Baskar, P.
10/087573
Search notes.

- key terms

(FILE 'HCAPLUS' ENTERED AT 09:28:17 ON 21 NOV 2003)
L2 122 SEA FILE=HCAPLUS ABB=ON PLU=ON (BABESIA OR B)(W)CANIS
L4 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (15KD? OR 15KILOD? OR KILOD? OR KILO(W)(DA OR DALTON) OR KDA?)

L4 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:742422 HCAPLUS
TITLE: Molecular characterization of a gene encoding a 29-**kDa** cytoplasmic protein of Babesia gibsoni and evaluation of its diagnostic potentiality
AUTHOR(S): Fukumoto, Shinya; Xuan, Xuenan; Inoue, Noboru; Igarashi, Ikuo; Sugimoto, Chihiro; Fujisaki, Kozo; Nagasawa, Hideyuki; Mikami, Takeshi; Suzuki, Hiroshi
CORPORATE SOURCE: National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido, 080-8555, Japan
SOURCE: Molecular and Biochemical Parasitology (2003), 131(2), 129-136
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cDNA expression library prepared from Babesia gibsoni merozoite mRNA was screened with B. gibsoni-infected dog serum. cDNA encoding 29-**kDa** protein was cloned and designated as the P29 gene. The complete nucleotide sequence of the P29 gene was 792 bp. Computer anal. suggested that the sequence of the P29 gene contained an open reading frame of 597 bp with a coding capacity of approx. 23.4 **kDa** and a single intron of 250 bp. The P29 protein had homol. to Toxoplasma gondii cytoskeletal protein IMC1. Southern blot anal. indicated that the P29 gene was present as a single copy in the B. gibsoni genome. The native P29 protein of B. gibsoni with a mol. mass of 29 **kDa** was identified by Western blotting with anti-recombinant P29 mouse serum. Confocal laser microscopic anal. showed that the P29 protein was located on the cytoplasma of B. gibsoni merozoites. The recombinant P29 protein expressed in E. coli was used as an antigen in an ELISA (ELISA). The ELISA was able to differentiate between B. gibsoni-infected dog serum and **B. canis** subspecies-infected dog serum or normal dog serum. Furthermore, the antibody response against the P29 protein was maintained during the chronic stage of infection in an exptl. infected dog, indicating that the recombinant P29 protein might be a useful diagnostic reagent for the detection of antibodies to B. gibsoni in dogs.

L4 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:573313 HCAPLUS
DOCUMENT NUMBER: 139:81638
TITLE: Immunoassay for detection of Brucella canis infection using antigen extract in diagnostic kit
INVENTOR(S): Nascimento, Roberto Meyer; Freire, Songeli Menezes; Melo, Stella Maria Barouin; Ribeiro, Marcos Borges
PATENT ASSIGNEE(S): Universidade Federal da Bahia, Brazil;

Laboratorio De Imunologia E Biologia Molecular of Instituto De Ciencias Da Saude
SOURCE: Braz. Pedido PI, 38 pp.
CODEN: BPXXDX
DOCUMENT TYPE: Patent
LANGUAGE: Portuguese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BR 2001004180	A	20020528	BR 2001-4180	20010924

PRIORITY APPLN. INFO.: AR 2000-104960 A 20000922

AB An invention involving an immunol. test to detect Brucella canis infection in patients susceptible to infection by **B. canis**. To perform the test a sample of body fluid is put in contact with a soluble antigen extract from Brucella canis. The antigen exts. are characterized by containing antigens from either of two groups: (a) antigens of mol. weight of 61 **kDa** and 55 **kDa** obtained by heating Brucella canis bacteria or (b) antigens of mol. weight of 46 **kDa**, 38 **kDa** and 28 **kDa**, obtained by exposing the bacteria to ultrasound. The extract is immobilized on a test surface, the surface is blocked to minimize non-specific bindings, biol. fluids from the patient are added to the surface, antibody conjugated and anti-Igs (from human or dogs) are added, the surfaced is washed and the conjugated antibodies are identified. The test may be used in diagnostic kits, to be used for the detection of Brucella in dogs, humans or cattle.

L4 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:693163 HCAPLUS
DOCUMENT NUMBER: 137:231343
TITLE: **Babesia canis**-derived 15 **kDa** and 32 **kDa** proteins for use in vaccine compositions
INVENTOR(S): Schetters, Theodorus Petrus Maria; Carcy, Bernard Pierre Dominique; Drakulovski, Pascal Robert; Gorenflot, Andre Francois
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238983	A1	20020911	EP 2002-75830	20020304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 2002001446	A	20020902	ZA 2002-1446	20020220
JP 2002360285	A2	20021217	JP 2002-42621	20020220
US 2003165872	A1	20030904	US 2002-87573	20020228

PRIORITY APPLN. INFO.: EP 2001-200816 A 20010306

AB The present invention relates to nucleic acid sequences encoding novel **Babesia canis** associated proteins and to cDNA fragments, recombinant DNA mols. and live recombinant carriers

comprising these sequences. Furthermore, the invention relates to host cells comprising such nucleic acid sequences, cDNA fragments, recombinant DNA mols. and live recombinant carriers. Also, the invention relates to proteins encoded by these nucleotide sequences, to vaccines for combating **Babesia canis** infections comprising these proteins or genetic material encoding these proteins and methods for the preparation of vaccines. Another embodiment of the invention relates to these **Babesia canis** associated proteins for use in vaccines and to the use of the **Babesia canis** associated proteins in the manufacture of vaccines. Finally, the invention relates to diagnostic tools for the detection of **Babesia canis** associated nucleic acid sequences, for the detection of antibodies against **Babesia canis** associated antigenic material.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:550024 HCAPLUS
DOCUMENT NUMBER: 136:273849
TITLE: Identification and expression of a 50-**kilodalton** surface antigen of Babesia gibsoni and evaluation of its diagnostic potential in an enzyme-linked immunosorbent assay
AUTHOR(S): Fukumoto, Shinya; Xuan, Xuenan; Nishikawa, Yoshifumi; Inoue, Noboru; Igarashi, Ikuo; Nagasawa, Hideyuki; Fujisaki, Kozo; Mikami, Takeshi
CORPORATE SOURCE: National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Hokkaido, 080-8555, Japan
SOURCE: Journal of Clinical Microbiology (2001), 39(7), 2603-2609
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cDNA expression library prepared from Babesia gibsoni merozoite mRNA was screened with B. gibsoni-infected dog serum. CDNA encoding a 50-**kDa** protein was cloned and designated the P50 gene. The complete nucleotide sequence of the P50 gene was 1,922 bp. Computer anal. suggested that the sequence of the P50 gene contained an open reading frame of 1,401 bp with a coding capacity of approx. 50 **kDa**. The complete genomic nucleotide sequence of the P50 gene has been analyzed and shown to contain a single intron of 37 bp. Southern blotting anal. indicated that the P50 gene was present at a single copy in the B. gibsoni genome. The native P50 protein of B. gibsoni with a mol. mass of 50 **kDa** was identified by Western blotting with anti-recombinant P50 mouse serum. Confocal laser microscopic anal. showed that the P50 protein was located on the surface of B. gibsoni merozoites. The recombinant P50 protein expressed by baculovirus in insect cells was used as the antigen in an ELISA. The ELISA was able to differentiate between B. gibsoni-infected dog serum and **B. canis**-infected dog serum or noninfected dog serum. Furthermore, the antibody response against the recombinant P50

protein was maintained until the chronic stage of infection in dogs exptl. infected with B. gibsoni was developed. These results demonstrate that the recombinant P50 protein might be a useful diagnostic reagent for detection of antibodies to B. gibsoni in dogs.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:716810 HCAPLUS
DOCUMENT NUMBER: 132:46701
TITLE: Characterization and molecular cloning of an adenosine kinase from **Babesia canis** rossi
AUTHOR(S): Carret, Celine; Delbecq, Stephane; Labesse, Gilles; Carcy, Bernard; Precigout, Eric; Moubri, Karina; Schetters, Theo P. M.; Gorenflot, Andre
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire, EA MESR 2413, UFR des Sciences Pharmaceutiques et Biologiques, Montpellier, F-34060, Fr.
SOURCE: European Journal of Biochemistry (1999), 265(3), 1015-1021
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the search for immunoprotective antigens of the intraerythrocytic **Babesia canis** rossi parasite, a new cDNA was cloned and sequenced. Protein sequence database searches suggested that the 41-**kDa** protein belongs to the phosphofructokinase B type family (PFK-B). However, because of the low level sequence identity (< 20%) of the protein both with adenosine and sugar kinases from this family, its structural and functional features were further investigated using mol. modeling and enzymic assays. The sequence/structure comparison of the protein with the crystal structure of a member of the PFK-B family, Escherichia coli ribokinase (EcRK), suggested that it might also form a stable and active dimer and revealed conservation of the ATP-binding site. However, residues specifically involved in the ribose-binding sites in the EcRK sequence (S and N) were substituted in its sequence (by H and M, resp.), and were suspected of binding adenosine compds. rather than sugar ones. Enzymic assays using a purified glutathione S-transferase fusion protein revealed that this protein exhibits rapid catalysis of the phosphorylation of adenosine with an apparent Km value of 70 nM, whereas it was inactive on ribose or other carbohydrates. As enzymic assays confirmed the results of the structure/function anal. indicating a preferential specificity towards adenosine compds., this new protein of the PFK-B family corresponds to an adenosine kinase from **B. canis** rossi. It was named BcrAK.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:460047 HCAPLUS

DOCUMENT NUMBER: 129:227846
TITLE: Comparative analysis of Brucella antigen by immunoblotting with specific sera of immunized rabbits
AUTHOR(S): Kulakov, Yu. K.; Zheludkov, M. M.; Lavrova, V. A.; Dranovskaya, E. A.; Skavronskaya, A. G.
CORPORATE SOURCE: NII Epidemiol. Mikrobiol. im. Gamalei, RAMN, Moscow, Russia
SOURCE: Molekulyarnaya Genetika, Mikrobiologiya i Virusologiya (1998), (2), 7-13
CODEN: MGMVDU; ISSN: 0208-0613
PUBLISHER: Meditsina
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Brucella antigens recognized by IgG antibodies in cell lysates from various Brucella species differing by the origin, biol., and virulent properties (including the reference, vaccine, and newly isolated strains) were compared by SDS-PAGE. Proteins in SDS-cell lysates were separated by 12% SDS-PAGE and protein gels were stained with Coomassie brilliant blue R-250 and Silver reagent. SDS-PAGE showed differences in the protein profiles of 15 strains of different species. Immunoblotting revealed that rabbit S-antisera contained IgG reacting with S-LPS and identical proteins of 90 to 16 **kDa** belonging to B. melitensis, B. abortus, and B. neotomae strains. **B. canis** strains had 4 antigens reacting with these antisera, whereas B. ovis had none. No agglutinating antibody were detected by the standard tube agglutination test with smooth Brucella strains in rabbit R-antisera. By contrast, immunoblotting anal. with these sera demonstrated common 90-16 **kDa** antigens in the strains of B. melitensis, B. suis, B. abortus, B. neotomae, and **B. canis**. B. ovis possessed none of these antigens. Thus, all Brucella species except B. ovis possess common protein antigens reacting with IgG.

L4 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:860102 HCAPLUS
DOCUMENT NUMBER: 123:277649
TITLE: Restriction site polymorphism of the genes encoding the major 25 **kDa** and 36 **kDa** outer membrane proteins of Brucella
AUTHOR(S): Cloeckaert, Axel; Verger, Jean-Michel; Grayon, Maggy; Grepinet, Olivier
CORPORATE SOURCE: Laboratoire de Pathologie Infectieuse et Immunologie, Institut National de la Recherche Agronomique, Nouzilly, 37380, Fr.
SOURCE: Microbiology (Reading, United Kingdom) (1995), 141(9), 2111-21
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Seventy-seven Brucella reference and field strains from different geog. origins and hosts representing the 6 recognized species and their different biovars were analyzed for diversity of their genes encoding the major 25 and 36 **kDa** outer-membrane proteins (OMPs) by PCR-RFLP. The 25-**kDa** OMP is encoded by a single gene (omp25), whereas 2 closely related genes (omp2a and omp2b) encode and potentially express the 36-**kDa** OMP. Anal. of

PCR products of the omp25 gene digested with 9 restriction enzymes revealed 2 species-specific markers, i.e. the absence of the EcoRV site in all Brucella melitensis strains and an .apprx.50 bp deletion at the 3' terminal end of the gene in all Brucella ovis strains. Anal. of PCR products of the omp2a and omp2b genes digested with 13 restriction enzymes indicated a greater diversity than the omp25 gene among the 6 Brucella species and within the Brucella abortus, Brucella suis, B. melitensis, and B. ovis species. Greater polymorphism was also detected for the omp2b than for the omp2a gene, especially in B. ovis which seemed to carry 2 similar (but not identical) copies of omp2a instead of one copy each of omp2a and omp2b for the other Brucella species as was previously suggested by Ficht et al. (1990). Results of PCR-RFLP indicated that distinction can be made between Brucella species and some of their biovars, except between **B. canis** and B. suis bv. 3 and 4, on the basis of the size and diversity of their major OMP genes, and that it could be of importance for diagnostic, epidemiol., and evolutionary study purposes.

L4 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:832227 HCAPLUS
DOCUMENT NUMBER: 123:225425
TITLE: Surface exposure of outer membrane protein and lipopolysaccharide epitopes in Brucella species studied by enzyme-linked immunosorbent assay and flow cytometry
AUTHOR(S): Bowden, Raul A.; Cloeckaert, Axel; Zygmunt, Michel S.; Bernard, Serge; Dubray, Gerard
CORPORATE SOURCE: Laboratoire de Pathologie Infectieuse et Immunologie, Centre de Recherches de Tours, Nouzilly, 37380, Fr.
SOURCE: Infection and Immunity (1995), 63(10), 3945-52
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB OMPs were shown to be more accessible to monoclonal antibodies (MAbs) on rough (R) Brucella melitensis and B. abortus strains than to MAbs on their smooth (S) counterparts. Here, the authors have extended this study to representatives of the main Brucella species, using MAbs specific for OMPs and S and R lipopolysaccharides (S-LPS and R-LPS). ELISA, flow cytometry, and immunoelectron microscopy showed important differences between strains in the binding of OMP- and R-LPS-specific MAbs which were in part related to the particular expression of S-LPS, irresp. of the species. Results indicated that both the amount and the length of O polysaccharide on S-LPS greatly influenced the accessibility of OMP and R-LPS epitopes to MAbs. S-R B. melitensis EP and S B. suis 40, for instance, which express O-polysaccharide chains in small amts. and with short mean length, resp., bound a greater number of OMP- and R-LPS-specific Mabs than the other S Brucella strains. The major 31-34-**kDa** OMP was the most exposed OMP on S strains of B. melitensis and B. suis. In most cases, flow cytometry results agreed with those of ELISA and supplied addnl. data, such as the homogeneity or heterogeneity of OMP expression at the strain level. However, there were some discordances between flow cytometry and ELISA results concerning the surface exposure of the 25-27-**kDa** and 31-34-**kDa** OMPs on S strains and that of minor OMPs in vaccine strain B.

melitensis Rev.1. Immunoelectron microscopy confirmed the poor accessibility of OMPs to MAbs on the surface of S Brucella strains. The naturally R pathogenic species B. ovis and **B. canis** bound the majority of OMP-specific MAbs as well as the R-LPS-specific MAbs. Therefore, the conserved OMP and R-LPS epitopes could play a role as targets of protective antibody-mediated immunity in infections caused by naturally R B. ovis and **B. canis**.

L4 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:647459 HCAPLUS
DOCUMENT NUMBER: 121:247459
TITLE: Identification of an immunoreactive Brucella abortus HtrA stress response protein homolog
AUTHOR(S): Roop, R. Martin, II; Fletcher, Terry W.; Sriranganathan, Nammalwar M.; Boyle, Stephen M.; Schurig, Gerhardt G.
CORPORATE SOURCE: Med. Cent., Louisiana State Univ., Shreveport, LA, 71130-3932, USA
SOURCE: Infection and Immunity (1994), 62(3), 1000-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An 11-kb fragment of Brucella abortus genomic DNA cloned into the BamHI site of pUC9 expressed a 60-**kDa** protein in Escherichia coli DH5-α. Antibodies reactive with this 60-**kDa** protein were detected by Western blot (immunoblot) anal. in sera from mice, cattle, and goats exptl. infected with B. abortus, in sera from mice exptl. infected with Brucella melitensis, and in serum from a dog exptl. infected with Brucella canis. Similar results were seen with sera obtained from cattle and dogs with naturally acquired brucellosis. The gene encoding the 60-**kDa** Brucella protein was localized to a 2-kb EcoRI fragment which was also reactive in Southern blots with genomic DNA from other strains of B. abortus as well as with genomic DNA from B. melitensis and **B. canis**. Nucleotide sequence anal. of the cloned EcoRI fragment revealed an open reading frame encoding a protein with a predicted mol. mass of 51,847 Da and an isoelec. point of 5.15. Comparison of the deduced amino acid sequence of the immunoreactive Brucella protein with the SWISS-PROT protein sequence data base revealed that it shares >40% amino acid sequence identity with the E. coli and Salmonella typhimurium HtrA stress response proteins. Computer-assisted anal. of this amino acid sequence also predicted that the putative Brucella HtrA homolog contains an export signal sequence and a serine protease active site, two structural features characteristic of previously described HtrA proteins. A potential σE type heat shock promoter sequence was detected upstream of the cloned Brucella htrA gene, and Northern (RNA) blot anal. demonstrated that exposure of B. abortus 2308 to heat shock conditions resulted in a transient elevation of htrA transcription. These results strongly suggest that the immunoreactive 60-**kDa** Brucella protein is a member of the HtrA class of stress response proteins.

L4 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:487893 HCAPLUS
DOCUMENT NUMBER: 119:87893
TITLE: Characterization of a family of multi-copy genes

encoding rhoptry protein homologs in Babesia bovis, Babesia ovis, and **Babesia canis**

AUTHOR(S): Dalrymple, Brian P.; Casu, Rosanne E.; Peters, Jennifer M.; Dimmock, Christine M.; Gale, Kevin R.; Boese, Reinhard; Wright, Ian G.

CORPORATE SOURCE: Div. Trop. Anim. Prod., Commonw. Sci. Ind. Res. Org., Indooroopilly, Australia

SOURCE: Molecular and Biochemical Parasitology (1993), 57(2), 181-92
CODEN: MBIPDP; ISSN: 0166-6851

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody that had been raised against a protease-containing fraction of B. bovis, and shown to bind to a protein located in the rhoptries, was used to screen a B. bovis cDNA expression library. The sequence of the protein encoded by a pos. clone was almost identical to the equivalent region of a previously described B. bovis 60-**kDa** rhoptry protein (Bv60). A tandem repeat of the gene encoding Bv60 was identified in all Australian isolates of B. bovis examined Genes encoding homologs of Bv60 were cloned from B. ovis and **B. canis**. In B. ovis, 5 closely linked genes were identified. Four of these genes appeared to encode very similar proteins (Bo60.1-4). The protein (Bo60.5) encoded by the 5th B. ovis gene had 72% amino acid identity to Bo60.1-4 in the N-terminal 306 amino acids, but no significant similarities in the C-terminal region. In **B. canis** one gene (Bc60.2) was sequenced and a second closely linked gene was identified. A further member of the family, p58, has also been described previously from Babesia bigemina. Tandemly repeated genes subject to extensive gene conversion appear to be a feature of this family of babesial rhoptry protein homologs. No proteins significantly related to any members of the gene family were identified in a search of translated DNA and protein sequence databases. Thus the function of this family of proteins remains a matter for speculation.

L4 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1993:186062 HCAPLUS

DOCUMENT NUMBER: 118:186062

TITLE: Molecular cloning and nucleotide sequence analysis of the gene encoding the immunoreactive Brucella abortus Hsp60 protein, BA60K

AUTHOR(S): Roop, R. Martin, II; Price, Michelle L.; Dunn, Bruce E.; Boyle, Stephen M.; Sriranganathan, Nammalwar; Schurig, Gerhardt G.

CORPORATE SOURCE: Dep. Microbiol., Univ. Arkansas Med. Sci., Little Rock, AR, 72205, USA

SOURCE: Microbial Pathogenesis (1992), 12(1), 47-62
CODEN: MIPAEV; ISSN: 0882-4010

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A recombinant 60 **kDa** B. abortus protein expressed in Escherichia coli was recognized in immunoblots by sera from mice exptl. infected with B. abortus and a dog exptl. infected with **B. canis**. Sera from humans and dogs with naturally acquired brucellosis also recognized this protein, which was designated BA60K. The gene encoding BA60K was localized within

an 18-kb B. abortus genomic fragment and its direction of transcription determined by subcloning and maxicell anal. of selected restriction fragments. The nucleotide sequence of 1800 bases encompassing the predicted gene location was determined, revealing an open reading frame encoding a protein of 546 amino acids (predicted relative mol. mass of 57,515). Solid-phase microsequencing of BA60K eluted from two-dimensional polyacrylamide gels confirmed the predicted amino acid sequence. Comparison of the predicted amino acid sequence of BA60K with a protein sequence database revealed that BA60K shares 67.9% identity with the GroEL protein of E. coli, a member of the Hsp60 family of chaperonins. The immunodominant Hsp60 homologs from Legionella pneumophila, Chlamydia trachomatis, and Mycobacterium tuberculosis were also found to share greater than 59% amino acid sequence identity with the BA60K protein. The identification of BA60K as a member of the Hsp60 family of chaperonins supports its role in stimulating a prominent host immune response during the course of Brucella infections. It also indicates that BA60K is an important candidate for studies aimed at identifying the antigens responsible for eliciting the protective immune response to brucellosis.

L4 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:495076 HCAPLUS
DOCUMENT NUMBER: 111:95076
TITLE: Characterization of Brucella canis protein antigens and polypeptide antibody responses of infected dogs
AUTHOR(S): Carmichael, Leland E.; Joubert, Jean C.; Jones, Laura
CORPORATE SOURCE: Baker Inst. Anim. Health, New York State Coll. Vet. Med., Ithaca, NY, 14853, USA
SOURCE: Veterinary Microbiology (1989), 19(4), 373-87
CODEN: VMICDQ; ISSN: 0378-1135
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cytoplasmic protein antigens (CPAg) of Brucella canis were characterized by SDS-PAGE and anal. of 35S-labeled polypeptides. Approx. mol. wts. of the immunoreactive polypeptides were determined by migration patterns of the immunopptd. polypeptides after SDS-PAGE or Western immunoblotting of sera collected at various times after exptl. infection of dogs. Polypeptides were specifically precipitated by sera of infected dogs, but not from the sera of normal or false-pos. (seropos., non-infected) animals. During the initial month after infection, proteins with mol. wts. s (MW) of .apprx.18, 22, 31, 42 and 54 **kDa** were commonly recognized. A 20-**kDa** polypeptide was first recognized at 8-10 wk after infection, but it was detected inconsistently after 6 mos. Addnl. polypeptides detected from 2 to 12 mos. post-infection had MW of 22, 66-68 and, less regularly, 42, 60, 82, 100 and >200 **kDa**. The polypeptides most consistently recognized in sera from **B. canis**-infected dogs had MW of 18, 22, and 68 **kDa**.

L4 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:229687 HCAPLUS
DOCUMENT NUMBER: 110:229687
TITLE: Purification of Brucella canis cell wall antigen by using immunosorbent columns and use of the antigen in enzyme-linked immunosorbent assay for

specific diagnosis of canine brucellosis
AUTHOR(S): Serikawa, Tadao; Iwaki, Shuji; Mori, Masayuki; Muraguchi, Takehiko; Yamada, Junzo
CORPORATE SOURCE: Fac. Med., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Journal of Clinical Microbiology (1989), 27(5), 837-42
CODEN: JCMIDW; ISSN: 0095-1137
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cell wall antigen of **B. canis** was purified by immunosorbent columns. The antigen contained two proteins of 30 and 28 **kilodaltons** and a polysaccharide exhibiting a 12-**kilodalton** band upon 12.5% SDS-PAGE. Antibody to the purified antigen, which specifically reacted with the polysaccharide, was used as the first coating antibody in an ELISA for serol. diagnosis of canine brucellosis. Dogs inoculated orally with live **B. canis** were pos. and dogs from **B. canis**-free colonies were neg. in the ELISA. Results indicate that the ELISA is a specific serol. test for **B. canis** infection in dogs.

L4 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:149176 HCAPLUS
DOCUMENT NUMBER: 110:149176
TITLE: Recombinant alveolar surfactant protein
INVENTOR(S): Schilling, James W., Jr.; White, Robert T.; Cordell, Barbara; Benson, Bradley J.
PATENT ASSIGNEE(S): California Biotechnology, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8805820	A1	19880811	WO 1988-US92	19880115
W: AU, DK, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8812948	A1	19880824	AU 1988-12948	19880115
US 5169761	A	19921208	US 1991-699960	19910514
US 5385840	A	19950131	US 1992-965745	19921023
US 5430020	A	19950704	US 1993-74290	19930609
US 5840527	A	19981124	US 1995-483939	19950607

PRIORITY APPLN. INFO.:
US 1987-8453 A 19870129
US 1984-680358 A2 19841211
US 1985-808843 A2 19851213
US 1986-857715 A2 19860430
US 1987-117099 B2 19871104
WO 1988-US92 A 19880115
US 1988-266443 B2 19881101
US 1989-310035 B3 19890210
US 1989-430497 B1 19891101
US 1990-524360 A3 19900517
US 1991-639250 B1 19910107
US 1991-699960 A3 19910514
US 1993-116225 B1 19930902

US 1995-384609 B1 19950203

AB The cDNAs for human and dog 5 and 18 **kilodalton** (5K and 18K) alveolar surfactant proteins (ASPs) are cloned and sequenced. The human 5 and 18K cDNAs are expressed in CHO cells, and a fragment of the 18K protein is produced in Escherichia coli. The cDNAs encoding human ASPs with mol. wts. 18 and 5 **kilodaltons** (**kDa**) were cloned and expressed in CHO-K1 cells. ASP 32 **kDa** protein (recombinant or purified from tissue) was purified using a mannose-containing affinity column. In vivo tests with rabbit fetuses indicated that a mixture of phospholipids and human "10K" proteins (a mixture of 5 and 18 **kilodalton** and related proteins) is as effective as control surface active material prepared from rabbit lungs (Pins, compliance, and volume at specific pressures were determined).

L2 122 SEA FILE=HCAPLUS ABB=ON PLU=ON (BABESIA OR B)(W)CANIS
L5 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND 15K

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:08:05 ON 21 NOV 2003)
L6 48 S L4 OR L5
L7 17 DUP REM L6 (31 DUPLICATES REMOVED)

L7 ANSWER 1 OF 17 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003450971 IN-PROCESS
DOCUMENT NUMBER: 22875066 PubMed ID: 14511811
TITLE: Molecular characterization of a gene encoding a 29-**kDa** cytoplasmic protein of Babesia gibsoni and evaluation of its diagnostic potentiality.
AUTHOR: Fukumoto Shinya; Xuan Xuenan; Inoue Noboru; Igarashi Ikuo; Sugimoto Chihiro; Fujisaki Kozo; Nagasawa Hideyuki; Mikami Takeshi; Suzuki Hiroshi
CORPORATE SOURCE: National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080-8555, Japan.
SOURCE: MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (2003 Oct) 131 (2) 129-36.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
OTHER SOURCE: GENBANK-AB085585; GENBANK-AB085586
ENTRY DATE: Entered STN: 20030928
Last Updated on STN: 20031021

AB A cDNA expression library prepared from Babesia gibsoni merozoite mRNA was screened with B. gibsoni-infected dog serum. cDNA encoding 29-**kDa** protein was cloned and designated as the P29 gene. The complete nucleotide sequence of the P29 gene was 792 bp. Computer analysis suggested that the sequence of the P29 gene contained an open reading frame of 597 bp with a coding capacity of approximately 23.4 **kDa** and a single intron of 250 bp. The P29 protein had homology to Toxoplasma gondii cytoskeletal protein IMC1. Southern blot analysis indicated that the P29 gene was present as a single copy in the B. gibsoni genome. The native P29 protein of B. gibsoni with a molecular mass of 29 **kDa** was

identified by Western blotting with anti-recombinant P29 mouse serum. Confocal laser microscopic analysis showed that the P29 protein was located on the cytoplasma of B. gibsoni merozoites. The recombinant P29 protein expressed in E. coli was used as an antigen in an enzyme-linked immunosorbent assay (ELISA). The ELISA was able to differentiate between B. gibsoni-infected dog serum and **B . canis** subspecies-infected dog serum or normal dog serum. Furthermore, the antibody response against the P29 protein was maintained during the chronic stage of infection in an experimentally infected dog, indicating that the recombinant P29 protein might be a useful diagnostic reagent for the detection of antibodies to B. gibsoni in dogs.

L7 ANSWER 2 OF 17 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003067721 MEDLINE
DOCUMENT NUMBER: 22465710 PubMed ID: 12578313
TITLE: Serological diagnosis of brucellosis caused by Brucella canis.
AUTHOR: Ebani V V; Cerri D; Fratini F; Bey R F; Andreani E
CORPORATE SOURCE: Department of Animal Pathology, Prophylaxis and Food Hygiene, Faculty of Veterinary Medicine, University of Pisa, Viale delle Piagge, 2 - 56124 Pisa, Italy.
SOURCE: NEW MICROBIOLOGICA, (2003 Jan) 26 (1) 65-73. Journal code: 9516291. ISSN: 1121-7138.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (EVALUATION STUDIES) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030212 Last Updated on STN: 20030423 Entered Medline: 20030422

AB Blood serum samples from 2,328 dogs were tested to detect antibodies against Brucella canis with the agar gel immunodiffusion (AGID) and 2-mercaptoethanol slide agglutination test (ME-SAT) using Brucella ovis as the antigen. All blood serum samples were also evaluated for antibodies against Brucella abortus and Brucella melitensis using the Rose Bengal test. Twentyfive (1.07%) of the sera evaluated were considered positive with AGID test. Only 4 (16%) of these blood serum samples were positive when evaluated with ME-SAT. The 25 AGID positive samples and 25 AGID negative serum samples were also examined by: the complement fixation test (CFT) using B. ovis hot saline extract (HSE) as the antigen, indirect enzyme linked immunosorbent assay (ELISA) and immunoblotting (IB) using **B . canis** and B. ovis HSE antigens. Two positive canine sera from culture positive dogs and the serum of an experimentally RM6/66 **B. canis**-infected rabbit were employed as positive controls and one serum from a known uninfected dog as a negative control. ELISA with **B. canis** antigen gave 9 (18%) positive results (6 AGID-positive and 3 AGID-negative sera). ELISA performed with B. ovis antigen detected 15 (30%) positive samples (10 AGID-positive, 5 AGID-negative and 8 **B . canis** ELISA positive sera). IB analysis of known positive controls sera employing **B. canis** antigen detected bands with molecular weights of 94-80, 64-50, 35, 32-30, 28, 23, 20-18, 15-12 **kDa.** The same sera tested with B. ovis antigen revealed bands of 35, 32-30, 25, 23, 20-18,

15-12 **kDa**. No bands were observed with the negative control serum and the 50 canine tested sera.

L7 ANSWER 3 OF 17 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001366732 MEDLINE
DOCUMENT NUMBER: 21320765 PubMed ID: 11427577
TITLE: Identification and expression of a 50-**kilodalton** surface antigen of Babesia gibsoni and evaluation of its diagnostic potential in an enzyme-linked immunosorbent assay.
AUTHOR: Fukumoto S; Xuan X; Nishikawa Y; Inoue N; Igarashi I; Nagasawa H; Fujisaki K; Mikami T
CORPORATE SOURCE: National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido 080 to 8555, Japan.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (2001 Jul) 39 (7) 2603-9.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB051834
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB A cDNA expression library prepared from Babesia gibsoni merozoite mRNA was screened with B. gibsoni-infected dog serum. cDNA encoding a 50-**kDa** protein was cloned and designated the P50 gene. The complete nucleotide sequence of the P50 gene was 1,922 bp. Computer analysis suggested that the sequence of the P50 gene contained an open reading frame of 1,401 bp with a coding capacity of approximately 50 **kDa**. The complete genomic nucleotide sequence of the P50 gene has been analyzed and shown to contain a single intron of 37 bp. Southern blotting analysis indicated that the P50 gene was present at a single copy in the B. gibsoni genome. The native P50 protein of B. gibsoni with a molecular mass of 50 **kDa** was identified by Western blotting with anti-recombinant P50 mouse serum. Confocal laser microscopic analysis showed that the P50 protein was located on the surface of B. gibsoni merozoites. The recombinant P50 protein expressed by baculovirus in insect cells was used as the antigen in an enzyme-linked immunosorbent assay (ELISA). The ELISA was able to differentiate between B. gibsoni-infected dog serum and **B. canis**-infected dog serum or noninfected dog serum. Furthermore, the antibody response against the recombinant P50 protein was maintained until the chronic stage of infection in dogs experimentally infected with B. gibsoni was developed. These results demonstrate that the recombinant P50 protein might be a useful diagnostic reagent for detection of antibodies to B. gibsoni in dogs.

L7 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:201343 BIOSIS
DOCUMENT NUMBER: PREV200200201343
TITLE: The recombinant major antigenic protein 2 of

Ehrlichia canis: A potential diagnostic tool.
AUTHOR(S): Belanger, M. [Reprint author]; McSherry, L. J. [Reprint author]; Barbet, A. F. [Reprint author]; Breitschwerdt, E. D.; Sorenson, H. L. [Reprint author]; Bowie, M. V. [Reprint author]; Alleman, A. R. [Reprint author]
CORPORATE SOURCE: University of Florida, Gainesville, FL, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 246. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002

AB Ehrlichia canis, the etiologic agent of canine monocytic ehrlichiosis, has been reported throughout the world causing extensive morbidity and mortality. The Major Antigenic Protein 2 (map2) gene of E. canis was cloned in an expression vector and the recombinant protein was tested in ELISA for potential application in the serodiagnosis of canine monocytic ehrlichiosis. The recombinant MAP2 (rMAP2), which contained a C-terminal polyhistidine tag, had a molecular mass of approximately 26 **kDa**. The antigen was clearly identified by Western blots using antihistidine antibody and immune serum from an experimentally infected dog. The rMAP2 was tested by ELISA using 141 dogs serum samples known to be positive or negative as determined by immunoflorescence assay (IFA). Fifty-five of the serum samples were from dogs experimentally or naturally infected with E. canis. The remaining 86 serum samples were seronegative for E. canis but, to evaluate the specificity of the rMAP2 antigen, 33 of those were from dogs infected with **Babesia canis**, Ehrlichia platys, Ehrlichia ristici, Ehrlichia ewingii, Rickettsia rickettsii, Bartonella vinsonii, Haemobartonella canis, or Neospora caninum. The results obtained with the rMAP2 ELISA were compared with the IFA results. There was 100% agreement using IFA-positive samples from experimentally infected animals and a 97.3% agreement using IFA-positive samples from naturally infected animals. A 94.3% agreement using IFA-negative samples was obtained and no cross-reaction with serum from dogs infected with any of the other microorganisms tested were observed. Overall, there was a 97.2% agreement between the rMAP2 ELISA and the IFA. These data suggest that the rMAP2 of E. canis could be used in ELISA for the serodiagnosis of canine monocytic ehrlichiosis.

L7 ANSWER 5 OF 17 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999449606 MEDLINE
DOCUMENT NUMBER: 99449606 PubMed ID: 10518797
TITLE: Characterization and molecular cloning of an adenosine kinase from **Babesia canis** rossi.
AUTHOR: Carret C; Delbecq S; Labesse G; Carcy B; Precigout E; Moubri K; Schetters T P; Gorenflot A
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire,

Montpellier, France.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Nov) 265 (3) 1015-21.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ223322
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991214

AB In the search for immunoprotective antigens of the intraerythrocytic **Babesia canis** rossi parasite, a new cDNA was cloned and sequenced. Protein sequence database searches suggested that the 41-**kDa** protein belongs to the phosphofructokinase B type family (PFK-B). However, because of the low level sequence identity (< 20%) of the protein both with adenosine and sugar kinases from this family, its structural and functional features were further investigated using molecular modelling and enzymatic assays. The sequence/structure comparison of the protein with the crystal structure of a member of the PFK-B family, Escherichia coli ribokinase (EcRK), suggested that it might also form a stable and active dimer and revealed conservation of the ATP-binding site. However, residues specifically involved in the ribose-binding sites in the EcRK sequence (S and N) were substituted in its sequence (by H and M, respectively), and were suspected of binding adenosine compounds rather than sugar ones. Enzymatic assays using a purified glutathione S-transferase fusion protein revealed that this protein exhibits rapid catalysis of the phosphorylation of adenosine with an apparent Km value of 70 nM, whereas it was inactive on ribose or other carbohydrates. As enzymatic assays confirmed the results of the structure/function analysis indicating a preferential specificity towards adenosine compounds, this new protein of the PFK-B family corresponds to an adenosine kinase from **B. canis** rossi. It was named BcrAK.

L7 ANSWER 6 OF 17 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998274688 MEDLINE
DOCUMENT NUMBER: 98274688 PubMed ID: 9611754
TITLE: [Comparative analysis of antigens from different Brucella species using immunoblotting with antisera from immunized rabbits].
Sravnitel'nyi analiz antigenov razlichnykh vidov Brucella metodom immunoblota s antisyvorotkami immunizirovannykh krolikov.
AUTHOR: Kulakov Iu K; Zheludkov M M; Lavrova V A; Dranovskaia E A; Skavronskaia A G
SOURCE: MOLEKULIARNAIA GENETIKA, MIKROBIOLOGIA, I VIRUSOLOGA, (1998) (2) 7-13.
Journal code: 9315607. ISSN: 0208-0613.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811

Last Updated on STN: 19980811
Entered Medline: 19980727

AB Brucella antigens recognized by IgG antibodies in cell lysates from various Brucella species differing by the origin, biological, and virulent properties (including the reference, vaccine, and newly isolated strains) were compared by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Proteins in SDS-cell lysates were separated by 12% SDS-PAGE and protein gels were stained with Coomassie brilliant blue R-250 and Silver reagent. SDS-PAGE showed differences in the protein profiles of 15 strains of different species. Immunoblotting revealed that rabbit S-antisera contained IgG reacting with S-LPS and identical proteins of 90 to 16 **kDa** belonging to B, melitensis, B. suis, B. abortus, and B. neotomae strains. **B. canis** strains had 4 antigens reacting with these antisera, whereas B. ovis had none. No agglutinating antibody were detected by the standard tube agglutination test with smooth Brucella strains in rabbit R-antisera. By contrast, immunoblotting analysis with these sera demonstrated common 90-16 **kDa** antigens in the strains of B. melitensis, B. suis, B. abortus, B. neotomae, and **B. canis**. B. ovis possessed none of these antigens. These results confirm that all Brucella species except B. ovis possess common protein antigens reacting with IgG.

L7 ANSWER 7 OF 17 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 96009750 MEDLINE
DOCUMENT NUMBER: 96009750 PubMed ID: 7558303
TITLE: Surface exposure of outer membrane protein and lipopolysaccharide epitopes in Brucella species studied by enzyme-linked immunosorbent assay and flow cytometry.
AUTHOR: Bowden R A; Cloeckaert A; Zygmunt M S; Bernard S; Dubray G
CORPORATE SOURCE: Laboratoire de Pathologie Infectieuse et Immunologie, Centre de Recherches de Tours, Institut National de la Recherche Agronomique, Nouzilly, France.
SOURCE: INFECTION AND IMMUNITY, (1995 Oct) 63 (10) 3945-52. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951030

AB Seven surface-exposed outer membrane proteins (OMPs) in Brucella supp. have been previously described (A. Cloeckaert, P. de Wergifosse, G. Dubray, and J. N. Limet, Infect. Immun. 58:3980-3987, 1990). OMPs were shown to be more accessible to monoclonal antibodies (MAbs) on rough (R) Brucella melitensis and B. abortus strains than to MAbs on their smooth (S) counterparts. In this work, we have extended this study to representatives of the main Brucella species, using MAbs specific for OMPs and S and R lipopolysaccharides (S-LPS and R-LPS). Enzyme-linked immunosorbent assay (ELISA), flow cytometry, and immunoelectron microscopy showed important differences between strains in the binding of OMP- and R-LPS-specific MAbs which were in part related to the particular

expression of S-LPS, irrespective of the species. Results indicated that both the amount and the length of O polysaccharide on S-LPS greatly influenced the accessibility of OMP and R-LPS epitopes to MAbs. S-R B. melitensis EP and S B. suis 40, for instance, which express O-polysaccharide chains in small amounts and with short mean length, respectively, bound a greater number of OMP- and R-LPS-specific MAbs than the other S Brucella strains. The major 31- to 34-**kDa** OMP was the most exposed OMP on S strains of B. melitensis and B. suis. In most cases, flow cytometry results agreed with those of ELISA and supplied additional data, such as the homogeneity or heterogeneity of OMP expression at the strain level. However, there were some discordances between flow cytometry and ELISA results concerning the surface exposure of the 25- to 27-**kDa** and 31- to 34-**kDa** OMPs on S strains and that of minor OMPs in vaccine strain B. melitensis Rev.1. Immunoelectron microscopy confirmed the poor accessibility of OMPs to MAbs on the surface of S Brucella strains. The naturally R pathogenic species B. ovis and **B. canis** bound the majority of OMP-specific MAbs as well as the R-LPS-specific MAbs. Therefore, the conserved OMP and R-LPS epitopes could play a role as targets of protective antibody-mediated immunity in infections caused by naturally R B. ovis and **B. canis**.

L7 ANSWER 8 OF 17 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 96118691 MEDLINE
DOCUMENT NUMBER: 96118691 PubMed ID: 7496522
TITLE: Restriction site polymorphism of the genes encoding the major 25 **kDa** and 36 **kDa** outer-membrane proteins of Brucella.
AUTHOR: Cloeckaert A; Verger J M; Grayon M; Grepinet O
CORPORATE SOURCE: Laboratoire de Pathologie Infectieuse et Immunologie, Institut National de la Recherche Agronomique, Nouzilly, France.
SOURCE: MICROBIOLOGY, (1995 Sep) 141 (Pt 9) 2111-21. Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960116

AB Seventy-seven Brucella reference and field strains from different geographic origins and hosts representing the six recognized species and their different biovars were analysed for diversity of their genes encoding the major 25 and 36 **kDa** outer-membrane proteins (OMPs) by PCR-RFLP. The 25 **kDa** OMP is encoded by a single gene (omp25) whereas two closely related genes (omp2a and omp2b) encode and potentially express the 36 **kDa** OMP. Analysis of PCR products of the omp25 gene digested with nine restriction enzymes revealed two species-specific markers, i.e. the absence of the EcoRV site in all Brucella melitensis strains and an approximately 50 bp deletion at the 3' terminal end of the gene in all Brucella ovis strains. Analysis of PCR products of the omp2a and omp2b genes digested with 13 restriction enzymes indicated a greater diversity than the omp25 gene among the six Brucella species and within the Brucella abortus, Brucella suis, B. melitensis and B.

ovis species. Greater polymorphism was also detected for the omp2b than for the omp2a gene, especially in B. ovis which seemed to carry two similar (but not identical) copies of omp2a instead of one copy each of omp2a and omp2b for the other Brucella species as was previously suggested by Ficht et al. (1990; Mol Microbiol 4, 1135-1142). Results of PCR-RFLP indicated that distinction can be made between Brucellia species and some of their biovars, except between **B. canis** and B. suis bv. 3 and 4, on the basis of the size and diversity of their major OMP genes, and that it could be of importance for diagnostic, epidemiological and evolutionary study purposes.

L7 ANSWER 9 OF 17 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 96124051 MEDLINE
DOCUMENT NUMBER: 96124051 PubMed ID: 8570577
TITLE: Characterization and comparison of merozoite antigens of different **Babesia canis** isolates by serological and immunological investigations.
AUTHOR: Hauschild S; Shayan P; Schein E
CORPORATE SOURCE: Institut fur Parasitologie und Tropenveterinarmedizin, Freien Universitat Berlin, Germany.
SOURCE: PARASITOLOGY RESEARCH, (1995) 81 (8) 638-42. Journal code: 8703571. ISSN: 0932-0113.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960305

AB Merozoites of four **Babesia canis** isolates from Hungary, France, Africa, and Egypt were purified. Antigens were compared in an enzyme-linked immunosorbent assay (ELISA) and by immunoblotting. In the ELISA, antigen from the highly pathogenic isolate from Hungary showed the highest sensitivity for homologous and heterologous immune sera. This was confirmed by immunoblotting. Protein bands of the Hungarian isolate were strongly recognized by all **B. canis** immune sera, whereas the antigens from the other isolates showed only weak reactions with homologous and heterologous immune sera. Significant was a protein band of about 12 **kDa** appearing in all pathogenic isolates from Hungary, France, and South Africa but not in the apathogenic Egyptian isolate. This protein band may determine the virulence. For serological tests, the **B. canis** isolate from Hungary seems to be the one most suitable for detection of even mild infections.

L7 ANSWER 10 OF 17 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 95:730851 SCISEARCH
THE GENUINE ARTICLE: TA229
TITLE: CHARACTERIZATION AND COMPARISON OF MEROZOITE ANTIGENS OF DIFFERENT **BABESIA-CANIS** ISOLATES BY SEROLOGICAL AND IMMUNOLOGICAL INVESTIGATIONS
AUTHOR: HAUSCHILD S; SHAYAN P; SCHEIN E (Reprint)

CORPORATE SOURCE: FREE UNIV BERLIN, INST PARASITOL & TROPENVET MED, KONIGSWEG 67, D-14163 BERLIN, GERMANY (Reprint); FREE UNIV BERLIN, INST PARASITOL & TROPENVET MED, D-14163 BERLIN, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: PARASITOLOGY RESEARCH, (NOV 1995) Vol. 81, No. 8, pp. 638-642. ISSN: 0044-3255.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 12

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Merozoites of four **Babesia canis** isolates from Hungary, France, Africa, and Egypt were purified. Antigens were compared in an enzyme-linked immunosorbent assay (ELISA) and by immunoblotting. In the ELISA, antigen from the highly pathogenic isolate from Hungary showed the highest sensitivity for homologous and heterologous immune sera. This was confirmed by immunoblotting. Protein bands of the Hungarian isolate were strongly recognized by all **B, canis** immune sera, whereas the antigens from the other isolates showed only weak reactions with homologous and heterologous immune sera. Significant was a protein band of about 12 **kDa** appearing in all pathogenic isolates from Hungary, France, and South Africa but not in the apathogenic Egyptian isolate. This protein band may determine the virulence. For serological tests, the **B. canis** isolate from Hungary seems to be the one most suitable for detection of even mild infections.

L7 ANSWER 11 OF 17 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 94156447 MEDLINE
DOCUMENT NUMBER: 94156447 PubMed ID: 8112833
TITLE: Identification of an immunoreactive Brucella abortus HtrA stress response protein homolog.
AUTHOR: Roop R M 2nd; Fletcher T W; Sriranganathan N M; Boyle S M; Schurig G G
CORPORATE SOURCE: Department of Microbiology and Immunology, Louisiana State University Medical Center, Shreveport 71130-3932.
CONTRACT NUMBER: AI-28867 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1994 Mar) 62 (3) 1000-7. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L09274
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 20000303
Entered Medline: 19940330

AB An 11-kb fragment of Brucella abortus genomic DNA cloned into the BamHI site of pUC9 expressed a 60-**kDa** protein in Escherichia coli DH5-alpha. Antibodies reactive with this 60-**kDa** protein were detected by Western blot (immunoblot) analysis in sera from mice, cattle, and goats experimentally infected with B. abortus, in sera from mice experimentally infected

with Brucella melitensis, and in serum from a dog experimentally infected with Brucella canis. Similar results were seen with sera obtained from cattle and dogs with naturally acquired brucellosis. The gene encoding the 60-**kDa** Brucella protein was localized to a 2-kb EcoRI fragment which was also reactive in Southern blots with genomic DNA from other strains of B. abortus as well as with genomic DNA from B. melitensis and **B. canis**. Nucleotide sequence analysis of the cloned EcoRI fragment revealed an open reading frame encoding a protein with a predicted molecular mass of 51,847 Da and an isoelectric point of 5.15. Comparison of the deduced amino acid sequence of the immunoreactive Brucella protein with the SWISS-PROT protein sequence data base revealed that it shares > 40% amino acid sequence identity with the E. coli and Salmonella typhimurium HtrA stress response proteins. Computer-assisted analysis of this amino acid sequence also predicted that the putative Brucella HtrA homolog contains an export signal sequence and a serine protease active site, two structural features characteristic of previously described HtrA proteins. A potential sigma E type heat shock promoter sequence was detected upstream of the cloned Brucella htrA gene, and Northern (RNA) blot analysis demonstrated that exposure of B. abortus 2308 to heat shock conditions resulted in a transient elevation of htrA transcription. These results strongly suggest that the immunoreactive 60-**kDa** Brucella protein is a member of the HtrA class of stress response proteins.

L7 ANSWER 12 OF 17 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 93:737388 SCISEARCH
THE GENUINE ARTICLE: ML003
TITLE: BABESIA-DIVERGENS - CHARACTERIZATION OF A 17-**KDA** MEROZOITE MEMBRANE-PROTEIN
AUTHOR: PRECIGOUT E (Reprint); VALENTIN A; CARCY B; GORENFLOT A; NAKAMURA K I; AIKAWA M; SCHREVEL J
CORPORATE SOURCE: FAC PHARM MONTPELLIER, BIOL CELLULAIRE LAB, 15 AVE CHARLES FLAHAULT, F-34090 MONTPELLIER 01, FRANCE (Reprint); LAB BIOL CELLULAIRE, CNRS, URA 290, F-36000 POITIERS, FRANCE; CASE WESTERN RESERVE UNIV, INST PATHOL, CLEVELAND, OH, 44106; MUSEUM NATL HIST NAT, BIOL PARASITAIRE & CHIMIOTHERAPIE LAB, CNRS, URA 114, F-75231 PARIS 05, FRANCE
COUNTRY OF AUTHOR: FRANCE; USA
SOURCE: EXPERIMENTAL PARASITOLOGY, (DEC 1993) Vol. 77, No. 4, pp. 425-434.
ISSN: 0014-4894.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 33

L7 ANSWER 13 OF 17 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 93165069 MEDLINE
DOCUMENT NUMBER: 93165069 PubMed ID: 8433711
TITLE: Characterisation of a family of multi-copy genes encoding rhoptry protein homologues in Babesia bovis, Babesia ovis and **Babesia canis**.
AUTHOR: Dalrymple B P; Casu R E; Peters J M; Dimmock C M; Gale K R; Boese R; Wright I G
CORPORATE SOURCE: Commonwealth Scientific and Industrial Research

Organisation, Division of Tropical Animal Production, Indooroopilly, QLD, Australia.
SOURCE: MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (1993 Feb) 57 (2) 181-92.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L00958; GENBANK-L00959; GENBANK-L00960; GENBANK-L00961; GENBANK-M91168; GENBANK-M91169; GENBANK-M91170; GENBANK-M91171; GENBANK-M91172; GENBANK-M91173; GENBANK-M91174; GENBANK-M91175; GENBANK-M91176; GENBANK-M91177; GENBANK-M91178
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930402
Last Updated on STN: 19970203
Entered Medline: 19930317

AB A monoclonal antibody that had been raised against a protease-containing fraction of Babesia bovis, and shown to bind to a protein located in the rhoptries, was used to screen a B. bovis cDNA expression library. The sequence of the protein encoded by a positive clone was almost identical to the equivalent region of a previously described B. bovis 60-**kDa** rhoptry protein (Bv60). A tandem repeat of the gene encoding Bv60 was identified in all Australian isolates of B. bovis examined. Genes encoding homologous of Bv60 were cloned from Babesia ovis and **Babesia canis**. In B. ovis, 5 closely linked genes were identified. Four of these genes appeared to encode very similar proteins (Bo60.1-4). The protein (Bo60.5) encoded by the fifth B. ovis gene had 72% amino acid identity to Bo60.1-4 in the amino-terminal 306 amino acids, but no significant similarities in the carboxy-terminal region. In **B. canis** one gene (Bc60.2) was sequenced and a second closely linked gene was identified. A further member of the family, p58, has also been described previously from Babesia bigemina. Tandemly repeated genes subject to extensive gene conversion appear to be a feature of this family of babesial rhoptry protein homologous. No proteins significantly related to any members of the gene family were identified in a search of translated DNA and protein sequence databases. Thus the function of this family of proteins remains a matter for speculation.

L7 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 92219947 MEDLINE
DOCUMENT NUMBER: 92219947 PubMed ID: 1560753
TITLE: Molecular cloning and nucleotide sequence analysis of the gene encoding the immunoreactive Brucella abortus Hsp60 protein, BA60K.
AUTHOR: Roop R M 2nd; Price M L; Dunn B E; Boyle S M; Sriranganathan N; Schurig G G
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock 72205.
CONTRACT NUMBER: AI-28867 (NIAID)
SOURCE: MICROBIAL PATHOGENESIS, (1992 Jan) 12 (1) 47-62.
Journal code: 8606191. ISSN: 0882-4010.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920529
Last Updated on STN: 19920529
Entered Medline: 19920512

AB A recombinant 60 **kDa** Brucella abortus protein expressed in Escherichia coli was recognized in immunoblots by sera from mice experimentally infected with B. abortus and a dog experimentally infected with **B. canis**. Sera from humans and dogs with naturally acquired brucellosis also recognized this protein, which was designated BA60K. The gene encoding BA60K was localized within an 18 kb B. abortus genomic fragment and its direction of transcription determined by subcloning and maxicell analysis of selected restriction fragments. The nucleotide sequence of 1800 bases encompassing the predicted gene location was determined, revealing an open reading frame encoding a protein of 546 amino acids (predicted relative molecular mass of 57515). Solid phase micro-sequencing of BA60K eluted from two-dimensional polyacrylamide gels confirmed the predicted amino acid sequence. Comparison of the predicted amino acid sequence of BA60K with a protein sequence database revealed that BA60K shares 67.9% identity with the GroEL protein of E. coli, a member of the Hsp60 family of chaperonins. The immunodominant Hsp60 homologs from Legionella pneumophila, Chlamydia trachomatis and Mycobacterium tuberculosis were also found to share greater than 59% amino acid sequence identity with the BA60K protein. The identification of BA60K as a member of the Hsp60 family of chaperonins supports its role in stimulating a prominent host immune response during the course of Brucella infections. It also indicates that BA60K is an important candidate for studies aimed at identifying the antigens responsible for eliciting the protective immune response to brucellosis.

L7 ANSWER 15 OF 17 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 91017428 MEDLINE
DOCUMENT NUMBER: 91017428 PubMed ID: 2217119
TITLE: Characterization and purification of culture-derived soluble glycoproteins of **Babesia canis**.
AUTHOR: Azzar G; Radisson J; Got R
CORPORATE SOURCE: Laboratoire de Biochimie des Membranes (LBTM CNRS-UM 380024), Universite Claude Bernard Lyon, Villeurbanne, France.
SOURCE: PARASITOLOGY RESEARCH, (1990) 76 (7) 578-80.
Journal code: 8703571. ISSN: 0932-0113.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117
Last Updated on STN: 19910117
Entered Medline: 19901114

AB The addition of [14C]-glucosamine to media of **Babesia canis** cultures causes the appearance of labeled glycoproteins in the culture supernatants. These radioactive soluble glycoproteins were separated according to their molecular weight by gel filtration and according to their (acidic) pI by

preparative electrofocusing. The labeled fractions were then analyzed by SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis). The results showed three series of glycoproteic antigens. The molecular weights for the three antigens determined by gel filtration and by SDS-PAGE were approximately 100, 40, and 12.5 **kDa**, and the preparative gel electrofocusing suggested that the antigens focus in the pH range of 3-5.

L7 ANSWER 16 OF 17 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 89309211 MEDLINE
DOCUMENT NUMBER: 89309211 PubMed ID: 2473093
TITLE: Purification of a Brucella canis cell wall antigen by using immunosorbent columns and use of the antigen in enzyme-linked immunosorbent assay for specific diagnosis of canine brucellosis.
AUTHOR: Serikawa T; Iwaki S; Mori M; Muraguchi T; Yamada J
CORPORATE SOURCE: Institute of Laboratory Animals, Faculty of Medicine, Kyoto University, Japan.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1989 May) 27 (5) 837-42.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19960129
Entered Medline: 19890823

AB A cell wall antigen of Brucella canis was purified by immunosorbent columns. The antigen contained two proteins of 30 and 28 **kilodaltons** and a polysaccharide exhibiting a 12-**kilodalton** band upon 12.5% sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Antibody to the purified antigen, which specifically reacted with the polysaccharide, was used as the first coating antibody in an enzyme-linked immunosorbent assay (ELISA) for serological diagnosis of canine brucellosis. Dogs inoculated orally with live **B. canis** were positive and dogs from **B. canis**-free colonies were negative in the ELISA. Of 199 dogs from a brucellosis-contaminated area, 116 with negative titers in the tube agglutination test (TAT), using heat-inactivated whole **B. canis** cells as the antigen, were also negative in the ELISA. Seventy-eight of the dogs with questionable titers in the TAT were divided into two groups: 20 dogs that were positive in the ELISA and 58 that were negative. Of five dogs with positive titers in the TAT, three were positive in the ELISA and the gel immunodiffusion test (GD) with crude **B. canis** extract as the antigen and were also culture positive for **B. canis**. One dog was positive in the ELISA and GD but gave a negative culture result. Serum from the remaining dog, which was positive with high titer in the TAT but negative in the ELISA and in culture for **B. canis**, formed a spur precipitate with a homologous precipitate in the GD. These results indicate that the ELISA is a specific serological test for **B. canis** infection in dogs.

L7 ANSWER 17 OF 17 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 89318835 MEDLINE
DOCUMENT NUMBER: 89318835 PubMed ID: 2526408
TITLE: Characterization of Brucella canis protein antigens and polypeptide antibody responses of infected dogs.
AUTHOR: Carmichael L E; Joubert J C; Jones L
CORPORATE SOURCE: Baker Institute for Animal Health, Department of Veterinary Microbiology, Immunology and Parasitology, New York State College of Veterinary Medicine, Ithaca 14853.
SOURCE: VETERINARY MICROBIOLOGY, (1989 Apr) 19 (4) 373-87. Journal code: 7705469. ISSN: 0378-1135.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198908
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890821

AB The cytoplasmic protein antigens (CPAg) of Brucella canis were characterized by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and analysis of 35S-labeled polypeptides. Approximate molecular weights of the immunoreactive polypeptides were determined by migration patterns of the immunoprecipitated polypeptides after SDS-PAGE or Western immunoblotting of sera collected at various times after experimental infection of dogs. Polypeptides were specifically precipitated by sera of infected dogs, but not from the sera of normal or false-positive (seropositive, non-infected) animals. During the initial month after infection, proteins with molecular weight masses (MW) of approximately 18, 22, 31, 42 and 54 **kDa** were commonly recognized. A 20-**kDa** polypeptide was first recognized at 8-10 weeks after infection, but it was detected inconsistently after 6 months. Additional polypeptides detected from 2 to 12 months post-infection had MW of 22, 66-68 and, less regularly, 42, 60, 82, 100 and greater than 200 **kDa**. The polypeptides most consistently recognized in sera from **B. canis** -infected dogs had MW of 18, 22 and 68 **kDa**.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 10:13:30 ON 21 NOV 2003)

L9 211 S "SCHETTERS T"?/AU -Author(s)
L10 108 S "CARCY B"?/AU
L11 9 S "DRAKULOVSKI P"?/AU
L12 9 S L9 AND L10 AND L11
L13 37 S L9 AND (L10 OR L11)
L14 9 S L10 AND L11
L15 282 S L9 OR L10 OR L11
L16 65 S (L13 OR L15) AND L2
L17 65 S L11 OR L12 OR L14 OR L16
L18 20 DUP REM L17 (45 DUPLICATES REMOVED)

L18 ANSWER 1 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2003:237715 USPATFULL
TITLE: **Babesia canis** vaccine
INVENTOR(S): **Schetters, Theodorus Petrus Maria,** Cuyk, NETHERLANDS
Carcy, Bernard Pierre Dominique,

Montpellier, FRANCE
Drakulovski, Pascal Robert,
Montpellier, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003165872	A1	20030904
APPLICATION INFO.:	US 2002-87573	A1	20020228 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-200816	20010603

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: INTERVET INC, 405 STATE STREET, PO BOX 318, MILLSBORO, DE, 19966
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1761
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to nucleic acid sequences encoding novel **Babesia canis** associated proteins and to cDNA fragments, recombinant DNA molecules and live recombinant carriers comprising these sequences. Furthermore, the invention relates to host cells comprising such nucleic acid sequences, cDNA fragments, recombinant DNA molecules and live recombinant carriers. Also, the invention relates to proteins encoded by these nucleotide sequences, to vaccines for combating **Babesia canis** infections comprising these proteins or genetic material encoding these proteins and methods for the preparation of vaccines. Another embodiment of the invention relates to these **Babesia canis** associated proteins for use in vaccines and to the use of the **Babesia canis** associated proteins in the manufacture of vaccines. Finally the invention relates to diagnostic tools for the detection of **Babesia canis** associated nucleic acid sequences, for the detection of **Babesia canis** associated antigens and for the detection of antibodies against **Babesia canis** associated antigenic material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:191294 HCAPLUS
DOCUMENT NUMBER: 138:332679
TITLE: Antibodies raised against Bcvir15, an extrachromosomal double-stranded RNA-encoded protein from **Babesia canis**, inhibit the in vitro growth of the parasite
AUTHOR(S): **Drakulovski, P.**; **Carcy, B.**; Moubri, K.; Carret, C.; Depoix, D.; **Schetters, T. P. M.**; Gorenflot, A.
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire, EA MESR 2413, UFR des Sciences Pharmaceutiques et Biologiques, BP 14491, Montpellier, F-34093/5, Fr.
SOURCE: Infection and Immunity (2003), 71(3), 1056-1067

CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As part of a search for homologous members of the Plasmodium falciparum Pf60 multigene family in the intraerythrocytic protozoan parasite **Babesia canis**, we report here the characterization of a cDNA of 1,115 bp, which was designated Bcvir for its potential viral origin. The Bcvir cDNA contained two overlapping open reading frames (ORFs) (ORF1 from nucleotide [nt] 61 to 486 and ORF2 from nt 417 to 919), where Bcvir15, the deduced ORF1 peptide (M1 to I141), is the main expressed product. The Bcvir cDNA was derived from an extrachromosomal dsRNA element of 1.2 kbp that was always found associated with a double-stranded RNA (dsRNA) of 2.8 kbp by hybridization, and no copy of this cDNA sequence was found in **B. canis** genomic DNA. Biochem. characterization of Bcvir15, by using polyclonal rabbit sera directed against recombinant proteins, indicated that it is a soluble protein which remained associated with the cytoplasm of the **B. canis** merozoite. Interestingly, purified Igs from the anti-glutathione S-transferase-Bcvir15 (at a concentration of 160 μg/mL) induced 50% inhibition of the in vitro growth of **B. canis**, and the inhibitory effect was associated with morphol. damage of the parasite. Our data suggest that the extrachromosomal dsRNA-encoded Bcvir15 protein might interfere with the intracellular growth of the parasite rather than with the process of invasion of the host cell by the merozoite. Epitope mapping of Bcvir15 identified three epitopes that might be essential for the function of the protein.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:693163 HCAPLUS
DOCUMENT NUMBER: 137:231343
TITLE: **Babesia canis**-derived 15 kDa and 32 kDa proteins for use in vaccine compositions
INVENTOR(S): **Schetters, Theodorus Petrus Maria; Carcy, Bernard Pierre Dominique; Drakulovski, Pascal Robert**; Gorenflot, Andre Francois
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238983	A1	20020911	EP 2002-75830	20020304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 2002001446	A	20020902	ZA 2002-1446	20020220
JP 2002360285	A2	20021217	JP 2002-42621	20020220

US 2003165872 A1 20030904 US 2002-87573 20020228
PRIORITY APPLN. INFO.: EP 2001-200816 A 20010306

AB The present invention relates to nucleic acid sequences encoding novel **Babesia canis** associated proteins and to cDNA fragments, recombinant DNA mols. and live recombinant carriers comprising these sequences. Furthermore, the invention relates to host cells comprising such nucleic acid sequences, cDNA fragments, recombinant DNA mols. and live recombinant carriers. Also, the invention relates to proteins encoded by these nucleotide sequences, to vaccines for combating **Babesia canis** infections comprising these proteins or genetic material encoding these proteins and methods for the preparation of vaccines. Another embodiment of the invention relates to these **Babesia canis** associated proteins for use in vaccines and to the use of the **Babesia canis** associated proteins in the manufacture of vaccines. Finally, the invention relates to diagnostic tools for the detection of **Babesia canis** associated nucleic acid sequences, for the detection of antibodies against **Babesia canis** associated antigenic material.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:881244 HCAPLUS
DOCUMENT NUMBER: 138:181599
TITLE: Chromosome number, genome size and polymorphism of European and South African isolates of large Babesia parasites that infect dogs
AUTHOR(S): Depoix, D.; **Carcy, B.**; Jumas-Bilak, E.; Pages, M.; Precigout, E.; **Schetters, T. P. M.**; Ravel, C.; Gorenflot, A.
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire, EA MESR 2413, UFR des Sciences Pharmaceutiques et Biologiques, Montpellier, F-34093, Fr.
SOURCE: Parasitology (2002), 125(4), 313-321
CODEN: PARAAE; ISSN: 0031-1820
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pulsed-field gel electrophoresis of intact chromosomes from 2 isolates of each of the 2 most pathogenic species of large Babesia parasites that infect dogs, i.e. **Babesia canis** (European species) and B. rossi (South African species), revealed 5 chromosomes in their haploid genome. The size of chromosomes 1-5 was found to be different in the 2 species, ranging from 0.8 to 6.0 Mbp. The genome size was estimated to be approx. 14.5 Mbp for **B. canis** and 16 Mbp for B. rossi, resp. Within each species, the size of chromosomes 1-3 of **B. canis** and 1-2 of B. rossi was conserved between the 2 isolates, whereas the size of chromosomes 4-5 of **B. canis** and 3-5 of B. rossi was variable. Chromosomes 1-5 hybridized with a 28-mer telomeric oligonucleotide probe derived from Plasmodium berghei. When NotI-digested chromosomes of the 4 isolates were hybridized with the telomeric probe a maximum of 10 fragments was revealed. Moreover, hybridization of this telomeric probe to a Southern blot of genomic DNA from the 4 isolates, digested with a series of

restriction enzymes, revealed a species-specific restriction map. Hybridization of intact or NotI-digested chromosomes of both species with 2 sets of 3 cDNA-antigen probes derived from each species, revealed no cross-hybridization between these **B. canis** and B. rossi genes.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:609460 HCAPLUS
DOCUMENT NUMBER: 136:277691
TITLE: Vaccination of dogs against heterologous **Babesia canis** infection using antigens from culture supernatants
AUTHOR(S): **Schetters, T. P. M.**; Kleuskens, J. A. G. M.; Scholtes, N. C.; Gorenflot, A.; Moubri, K.; Vermeulen, A. N.
CORPORATE SOURCE: Parasitology R&D Department, Intervet International B.V., Boxmeer, Neth.
SOURCE: Veterinary Parasitology (2001), 100(1-2), 75-86
CODEN: VPARDI; ISSN: 0304-4017
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Soluble parasite antigens (SPA) from European **Babesia canis** can be used to protect dogs against a homologous but not heterologous challenge infection. In this study it is shown that when dogs are vaccinated with a mixture of SPA from both, a European **B. canis** isolate and a South African Babesia rossi isolate, protective immunity against heterologous **B. canis** infection is induced. Three groups of five beagle dogs each were vaccinated twice with graded doses of SPA derived from in vitro cultures of **B. canis** and B. rossi, with a 3-wk interval. Saponin was used as adjuvant. Three weeks after booster vaccination immunol. responsiveness against heterologous **B. canis** antigen was measured by seroconversion against infected erythrocytes and lymphocyte transformation using SPA. Upon vaccination dogs produced antibodies against infected erythrocytes and lymphoblastogenic responses against SPA in a dose-dependent manner. Dogs were then challenged with heterologous **B. canis** parasites. Dogs appeared to be protected against challenge infection, which was reflected in less severe decrease of packed cell volume (PCV) and reduced clin. signs. The level of protection to clin. signs (but not excessive PCV drop) was related to the level of SPA in plasma and spleen size, and not related to peripheral parasitemia. The results suggest that vaccination with this bivalent vaccine primes T-helper cells that recognize common epitopes on SPA from an antigenically distinct **B. canis** isolate. These cells provide the essential Th signal to mount an effective and timely antibody response against SPA and parasites or parasitised erythrocytes, which prevents the further development of clin. babesiosis.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 5

ACCESSION NUMBER: 2000:447918 BIOSIS
DOCUMENT NUMBER: PREV200000447918
TITLE: Babesia vaccine.
AUTHOR(S): **Schetters, Theodorus Petrus Mari** [Inventor, Reprint author]
CORPORATE SOURCE: Cuyk, Netherlands
ASSIGNEE: Akzo Nobel N.V., Arnhem, Netherlands
PATENT INFORMATION: US 6045806 April 04, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 4, 2000) Vol. 1233, No. 1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

AB The invention is directed to a vaccine comprising **Babesia canis** antigens from a strain of **Babesia canis** rossi and another **Babesia canis** subspecies. Such a vaccine gives both homologous protection, and heterologous protection to infection with strains other than those of which the antigens have been isolated. Preferably the antigens are soluble antigens which can be harvested from the supernatant of a culture of Babesia parasites.

L18 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:434655 BIOSIS
DOCUMENT NUMBER: PREV200000434655
TITLE: Vaccination of dogs against heterologous **Babesia canis** infection.
AUTHOR(S): **Schetters, Th.** [Reprint author]; Kleuskens, J. [Reprint author]; Scholtes, N. [Reprint author]; Vermeulen, A. [Reprint author]
CORPORATE SOURCE: Intervet International B. V., Boxmeer, Netherlands
SOURCE: Acta Parasitologica, (July, 2000) Vol. 45, No. 3, pp. 202. print.
Meeting Info.: VIII European Muticolloquium of Parasitology. Poznan, Poland. September 10-14, 2000. Witold Stefanski Institute of Parasitology.
ISSN: 1230-2821.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 2000
Last Updated on STN: 10 Jan 2002

L18 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1999:716810 HCAPLUS
DOCUMENT NUMBER: 132:46701
TITLE: Characterization and molecular cloning of an adenosine kinase from **Babesia canis** rossi
AUTHOR(S): Carret, Celine; Delbecq, Stephane; Labesse, Gilles; **Carcy, Bernard**; Precigout, Eric; Moubri, Karina; **Schetters, Theo P.**

M.; Gorenflot, Andre
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire, EA MESR 2413, UFR des Sciences Pharmaceutiques et Biologiques, Montpellier, F-34060, Fr.
SOURCE: European Journal of Biochemistry (1999), 265(3), 1015-1021
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the search for immunoprotective antigens of the intraerythrocytic **Babesia canis** rossi parasite, a new cDNA was cloned and sequenced. Protein sequence database searches suggested that the 41-kDa protein belongs to the phosphofructokinase B type family (PFK-B). However, because of the low level sequence identity (< 20%) of the protein both with adenosine and sugar kinases from this family, its structural and functional features were further investigated using mol. modeling and enzymic assays. The sequence/structure comparison of the protein with the crystal structure of a member of the PFK-B family, Escherichia coli ribokinase (EcRK), suggested that it might also form a stable and active dimer and revealed conservation of the ATP-binding site. However, residues specifically involved in the ribose-binding sites in the EcRK sequence (S and N) were substituted in its sequence (by H and M, resp.), and were suspected of binding adenosine compds. rather than sugar ones. Enzymic assays using a purified glutathione S-transferase fusion protein revealed that this protein exhibits rapid catalysis of the phosphorylation of adenosine with an apparent Km value of 70 nM, whereas it was inactive on ribose or other carbohydrates. As enzymic assays confirmed the results of the structure/function anal. indicating a preferential specificity towards adenosine compds., this new protein of the PFK-B family corresponds to an adenosine kinase from **B. canis** rossi. It was named BcrAK.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1999:424565 HCAPLUS
DOCUMENT NUMBER: 131:211361
TITLE: **Babesia canis** canis, **Babesia canis** vogeli, **Babesia canis** rossi: differentiation of the three subspecies by a restriction fragment length polymorphism analysis on amplified small subunit ribosomal RNA genes
AUTHOR(S): Carret, Celine; Walas, Fabien; **Carcy, Bernard**; Grande, Nathalie; Precigout, Eric; Moubri, Karina; **Schetters, Theo P.**; Gorenflot, Andre
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire et Moleculaire, EA MESR 2413, UFR des Sciences Pharmaceutiques et Biologiques, Montpellier, F-34060, Fr.
SOURCE: Journal of Eukaryotic Microbiology (1999),

46(3), 298-303
CODEN: JEMIED; ISSN: 1066-5234
PUBLISHER: Society of Protozoologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The parasites **Babesia canis** and Babesia gibsoni (phylum Apicomplexa) are responsible for canine babesiosis throughout the world. **Babesia canis** was previously described as a group of three biol. different subspecies, namely **B. canis** canis, **B. canis** vogeli, and **B. canis** rossi. We report partial sequences of small subunit rRNA gene (ssu-rDNA) of each subspecies amplified in vitro with primers derived from a semi-conserved region of the ssu-rDNA genes in other Babesia species. The polymerase chain reaction combined with a restriction fragment length polymorphism anal., using HinfI and TaqI restriction enzymes, confirmed the separation of **B. canis** into three subspecies. These sequences were compared with previously published sequences of other Babesia species. A phylogenetic approach showed that the three subspecies of **B. canis** belong to the clade of Babesia species sensu stricto where **B. canis** canis clusters with **B. canis** rossi whereas **B. canis** vogeli might form a monophyletic group with the cluster B. divergens and B. odocoilei. Our results show that the three subspecies of **B. canis** can readily be differentiated at the mol. level and suggest that they might be considered as true species.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 20 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 1998348527 MEDLINE
DOCUMENT NUMBER: 98348527 PubMed ID: 9683902

TITLE: Parasite localization and dissemination in the Babesia-infected host.

AUTHOR: **Schetters T P**; Kleuskens J; Scholtes N; Gorenflot A
CORPORATE SOURCE: Parasitology R & D Department, Intervet Int. b.v., Boxmeer, The Netherlands.. parasitology@intervet.akzonobel.nl

SOURCE: ANNALS OF TROPICAL MEDICINE AND PARASITOLOGY, (1998 Jun) 92 (4) 513-9. Ref: 25
Journal code: 2985178R. ISSN: 0003-4983.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980806

AB Babesia bovis infections in cattle and **B. canis** infections in dogs are characterized by non-haemolytic anaemia and low parasitaemia during the acute phase of the disease. In this phase of the disease, animals suffer from hypotension followed by

disturbances of the coagulation system. This review discusses the hypothesis that may explain the process of parasite localization in the host, and the consequences of such localization. It is suggested that hypotension favours the interaction between infected erythrocytes and the endothelial lining, thus facilitating localization of the infection. In addition, activation of the coagulation system by a parasite-derived molecule (one associated with the surface of infected erythrocytes or a soluble antigen) might consolidate this situation by causing cellular plugs to form. The continued proliferation of parasites in such plugs may then result in the occurrence of capillaries that are particularly heavily parasitised. An explanation is also suggested for the protective effect of vaccines against clinical babesiosis, based on the soluble parasite antigens that are released into the medium in cultures of babesial parasites.

L18 ANSWER 11 OF 20 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1998035367 MEDLINE
DOCUMENT NUMBER: 98035367 PubMed ID: 9368899
TITLE: Different **Babesia canis** isolates, different diseases.
AUTHOR: **Schetters T P**; Moubri K; Precigout E; Kleuskens J; Scholtes N C; Gorenflot A
CORPORATE SOURCE: Department of Parasitology, Intervet International BV, Boxmeer, The Netherlands.. parasitology@intervet.akzo.nl
SOURCE: PARASITOLOGY, (1997 Nov) 115 (Pt 5) 485-93. Journal code: 0401121. ISSN: 0031-1820.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980224
Last Updated on STN: 19980224
Entered Medline: 19980210

AB Using surface immunofluorescence isolate-specific antigens were detected on the membrane of erythrocytes infected with Babesia parasites. In addition, the strains reacted differently with Plasmagel in that the European isolate (B.c. canis) could be purified on Plasmagel effectively, whereas infected erythrocytes of the South-African isolate (B.c. rossi) could not. Experimental infection of dogs with **Babesia canis** isolates from geographically different areas revealed different pathology. The European isolate obtained from France exhibited transient parasitaemia, usually below 1%, associated with low PCV values and congestion of internal organs. Clinical disease was correlated with an effect on the coagulation system, and not with peripheral parasitaemia. Infection of dogs with South-African-derived isolate induced high parasitaemia usually much higher than 1%, which required chemotherapeutic treatment. In these animals clinical disease was correlated with peripheral parasitaemia and not with parameters of the coagulation system. The results show that the etiology of disease caused by these isolates of B.c. canis and B.c. rossi is different. This might have implications for the development of vaccines against these infections.

L18 ANSWER 12 OF 20 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 1998137977 MEDLINE
DOCUMENT NUMBER: 98137977 PubMed ID: 9477490
TITLE: Vaccination of dogs against **Babesia canis** infection.
AUTHOR: **Schetters T P**; Kleuskens J A; Scholtes N C; Pasman J W; Goovaerts D
CORPORATE SOURCE: Intervet International B.V., Department of Parasitology, Boxmeer, The Netherlands.
SOURCE: VETERINARY PARASITOLOGY, (1997 Dec 15) 73 (1-2) 35-41.
Journal code: 7602745. ISSN: 0304-4017.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980324

AB This paper describes the clinico-pathological parameters measured in dogs that were vaccinated against **Babesia canis** using soluble parasite antigens (SPA) and then challenged. The packed cell volume (PCV) and the plasma creatinine value decreased immediately after challenge. Actual PCV values could be predicted in the first 5-6 days of the infection, assuming that creatinine values were modulated by increase of plasma volume. This association no longer existed after that time, and observations indicated splenic involvement in reduction of numbers of circulating erythrocytes. The anaemia due to **B. canis** infection appears to be the result of a multifactorial process including plasma volume increase, erythrocyte retention in the spleen and erythrocyte destruction, partly due to parasite proliferation. Vaccination limited the reduction of PCV values, and the development of splenomegaly. Differences in protection between vaccinated and control animals became apparent 6 days after infection, when a memory immune response becomes operative, and the onset of recovery of vaccinated animals correlated with the onset of antibody production against SPA.

L18 ANSWER 13 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-059524 [07] WPIDS
DOC. NO. CPI: C1996-019868
TITLE: Vaccine against babesiosis in dogs - containing antigens from two sub-species of **Babesia canis**, providing homologous and heterologous protection.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): **SCHETTERS, T P M**
PATENT ASSIGNEE(S): (ALKU) AKZO NOBEL NV
COUNTRY COUNT: 10
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 691131	A1	19960110	(199607)*	EN	15
R: ES FR GR IT NL PT					
ZA 9505551	A	19960626	(199631)		27
HU 72403	T	19960429	(199742)		

IL 114443 A 19990714 (199935)
EP 691131 B1 19991006 (199946) EN
R: ES FR GR IT NL PT
ES 2141297 T3 20000316 (200021)
US 6045806 A 20000404 (200024)
HU 219314 B 20010328 (200124)#

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 691131	A1	EP 1995-201817	19950704
ZA 9505551	A	ZA 1995-5551	19950704
HU 72403	T	HU 1995-2051	19950705
IL 114443	A	IL 1995-114443	19950704
EP 691131	B1	EP 1995-201817	19950704
ES 2141297	T3	EP 1995-201817	19950704
US 6045806	A	US 1995-498550	19950705
HU 219314	B	HU 1995-2051	19950705

FILING DETAILS:

PATENT NO	KIND		PATENT NO
ES 2141297	T3	Based on	EP 691131
HU 219314	B	Previous Publ.	HU 72403

PRIORITY APPLN. INFO: EP 1994-201944 19940706
AN 1996-059524 [07] WPIDS
AB EP 691131 A UPAB: 19960222
Vaccine to protect dogs against babesiosis comprises antigens (Ag) from **Babesia canis** rossi and from another **B. canis** subspecies. The Babesia parasite are cultured in erythrocytes in a suitable nutrient medium, then Ag are recovered from the medium and mixed with appropriate excipients. Opt. the immunogenicity is increased by crosslinking or coupling Ag to a carrier, e.g. beta-galactosidase or protein A.
ADVANTAGE - The vaccine provides protection not only against the strains used for vaccination but also against heterologous strains.
Dwg.6/7

L18 ANSWER 14 OF 20 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 97366340 MEDLINE
DOCUMENT NUMBER: 97366340 PubMed ID: 9223150
TITLE: Not peripheral parasitaemia but the level of soluble parasite antigen in plasma correlates with vaccine efficacy against **Babesia canis**.
AUTHOR: **Schetters T P**; Scholtes N C; Kleuskens J A; Bos H J
CORPORATE SOURCE: Department of Parasitology, Intervet International BV, Boxmeer, The Netherlands.
SOURCE: PARASITE IMMUNOLOGY, (1996 Jan) 18 (1) 1-6. Journal code: 7910948. ISSN: 0141-9838.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 19971008
Entered Medline: 19970922

AB Groups of five dogs were vaccinated against **Babesia canis** using soluble parasite (SPA) antigens from in vitro cultures. Although vaccination did not significantly alter peripheral parasitaemia upon challenge, protected animals had lower levels of SPA in the plasma after a challenge infection. The severity of anaemia correlated with the SPA-load during the post-challenge period in that high levels of SPA were associated with low haematocrit values. In addition, it was found that recovery was associated with the production of antibodies against SPA. The results suggest that SPA induce anaemia during **B . canis** infection, and that vaccination with SPA results in antibody production that can neutralize the effects of SPA after a challenge infection.

L18 ANSWER 15 OF 20 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 95320956 MEDLINE
DOCUMENT NUMBER: 95320956 PubMed ID: 7597789
TITLE: Vaccine development from a commercial point of view.
AUTHOR: **Schetters T**
CORPORATE SOURCE: Intervet International bv, Parasitology R&D Department, Boxmeer, Netherlands.
SOURCE: VETERINARY PARASITOLOGY, (1995 Mar) 57 (1-3) 267-75. Journal code: 7602745. ISSN: 0304-4017.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19950817
Entered Medline: 19950803

AB The development of a commercial vaccine comprises distinct stages. Initiation of a research project is triggered by demands from the market. If commercial and technical requirements are met, a feasibility study is carried out. Research is started, and aimed at formulating the product profile (what the product looks like). The product profile is subject to requirements set by the market (e.g. whether the product will fit into existing vaccination schedules) and very often technical aspects affect the product profile (e.g. whether the freeze-dried product is easy to reconstitute). Only after a cost-profit analysis is positive, the development phase is entered. During this phase, experiments are carried out to obtain registration. After the product has been registered it is ready for production and marketing. Only few vaccines for hemoparasitic diseases have reached the market. These comprise: attenuated parasites (Toxoplasma gondii, Eimeria species); killed vaccines (Anaplasma marginale) and subunit vaccines (**Babesia canis**). Factors relating to the product potential of these vaccines are discussed.

L18 ANSWER 16 OF 20 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 95349971 MEDLINE
DOCUMENT NUMBER: 95349971 PubMed ID: 7542765
TITLE: Strain variation limits protective activity of

vaccines based on soluble **Babesia canis** antigens.

AUTHOR: **Schetters T H**; Kleuskens J; Scholtes N; Bos H J

CORPORATE SOURCE: Department of Parasitology, Intervet International B.V., Boxmeer, The Netherlands.

SOURCE: PARASITE IMMUNOLOGY, (1995 Apr) 17 (4) 215-8. Journal code: 7910948. ISSN: 0141-9838.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950911
Last Updated on STN: 19970203
Entered Medline: 19950831

AB Groups of five dogs were immunized with vaccines containing soluble parasite antigens (SPA) derived from in vitro culture of Babesis canis parasites, either obtained commercially (Pirodog) or produced at laboratory scale. Both vaccines generated antibodies that reacted with parasitised erythrocytes (PE). Upon challenge infection with homologous parasites, protection was evident from less severe decreases of haematocrit values, and reduced morbidity. Vaccinated animals, however, were not protected against challenge infection with heterologous **B. canis** parasites. Recovery from challenge infection coincided with the production of antibodies against parasitized erythrocytes. The results suggest that SPA from **B. canis** carry strain-specific determinants that are crucial for inducing protection in dogs against challenge infection, and explain vaccination failures in the field.

L18 ANSWER 17 OF 20 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 94353608 MEDLINE
DOCUMENT NUMBER: 94353608 PubMed ID: 8073606

TITLE: Vaccination of dogs against **Babesia canis** infection using antigens from culture supernatants with emphasis on clinical babesiosis.

AUTHOR: **Schetters T P**; Kleuskens J A; Scholtes N C; Pasman J W; Bos H J

CORPORATE SOURCE: Intervet International b.v., Parasitology R & D Department, Boxmeer, Netherlands.

SOURCE: VETERINARY PARASITOLOGY, (1994 Apr) 52 (3-4) 219-33. Journal code: 7602745. ISSN: 0304-4017.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941006
Last Updated on STN: 19970203
Entered Medline: 19940926

AB Groups of five dogs were vaccinated with **Babesia canis** antigens from in vitro culture in combination with saponin as adjuvant. Protection against challenge infection was evident as diminished clinical disease, decrease in parasitaemia, and a less marked fall in haematocrit values. Recovery from infection occurred at the time a memory immune response became

effective (from Days 5 to 6 after challenge infection onwards). The effect was dose dependent, the highest antigen dose being most effective. A lysate of normal erythrocytes did not have protective activity, indicating that a parasite component was responsible for protection. Unlike the malaria situation, disease was not associated with elevated levels of tumour necrosis factor in the plasma, nor with hypoglycaemia. Disease appeared to be the result of the activity of a parasite product, which could have triggered reactions which led to sequestration of erythrocytes from the peripheral venous blood. As a result, the packed cell volume decreased, and organs such as lymph nodes and spleen became congested. As soon as immunity had developed there was a rapid increase in the peripheral erythrocyte number, and congestion of the spleen diminished, indicative of restored capillary blood flow. The results further suggest that vaccination with a soluble parasite product blocks the trigger of this pathological process.

L18 ANSWER 18 OF 20 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 93:737388 SCISEARCH
THE GENUINE ARTICLE: ML003
TITLE: BABESIA-DIVERGENS - CHARACTERIZATION OF A 17-KDA MEROZOITE MEMBRANE-PROTEIN
AUTHOR: PRECIGOUT E (Reprint); VALENTIN A; **CARCY B**; GORENFLOT A; NAKAMURA K I; AIKAWA M; SCHREVEL J
CORPORATE SOURCE: FAC PHARM MONTPELLIER, BIOL CELLULAIRE LAB, 15 AVE CHARLES FLAHAULT, F-34090 MONTPELLIER 01, FRANCE (Reprint); LAB BIOL CELLULAIRE, CNRS, URA 290, F-36000 POITIERS, FRANCE; CASE WESTERN RESERVE UNIV, INST PATHOL, CLEVELAND, OH, 44106; MUSEUM NATL HIST NAT, BIOL PARASITAIRE & CHIMIOTHERAPIE LAB, CNRS, URA 114, F-75231 PARIS 05, FRANCE
COUNTRY OF AUTHOR: FRANCE; USA
SOURCE: EXPERIMENTAL PARASITOLOGY, (DEC 1993) Vol. 77, No. 4, pp. 425-434.
ISSN: 0014-4894.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 33

L18 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 92327120 MEDLINE
DOCUMENT NUMBER: 92327120 PubMed ID: 1625906
TITLE: Vaccination of dogs against **Babesia canis** infection using parasite antigens from in vitro culture.
AUTHOR: **Schetters T P**; Kleuskens J; Scholtes N; Bos H J
CORPORATE SOURCE: Department of Parasitology, Intervet International BV, Boxmeer, The Netherlands.
SOURCE: PARASITE IMMUNOLOGY, (1992 May) 14 (3) 295-305.
Journal code: 7910948. ISSN: 0141-9838.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920821

Searcher : Shears 308-4994

Last Updated on STN: 19970203
Entered Medline: 19920813

AB Groups of five dogs were vaccinated with different **Babesia canis** vaccine formulations. It appeared that partial protection against challenge infection was obtained when using parasite antigens from in vitro culture in combination with saponin. Protection was evident as a decrease in parasitaemia after challenge and was associated with the presence of serum antibodies against Babesia parasites. In addition, parasite antigen derived from in vitro culture supernatant exhibited more protective activity than somatic parasite antigen, in that a less marked fall of haematocrit values was found after challenge infection. The fall of haematocrit value observed in the animals immunized with somatic parasite antigen was not different from that observed in the adjuvant control group.

L18 ANSWER 20 OF 20 JAPIO (C) 2003 JPO on STN
ACCESSION NUMBER: 2002-360285 JAPIO
TITLE: **BABESIA CANIS** VACCINE
INVENTOR: **SCHETTERS THEODORUS PETRUS MARIA;**
CARCY BERNARD PIERRE DOMINIQUE;
DRAKULOVSKI PASCAL ROBERT; GORENFLOT ANDRE FRANCOIS
PATENT ASSIGNEE(S): AKZO NOBEL NV
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 2002360285	A	20021217	Heisei	C12N015-09

APPLICATION INFORMATION
STN FORMAT: JP 2002-42621 20020220
ORIGINAL: JP2002042621 Heisei
PRIORITY APPLN. INFO.: EP 2001-200816 20010306
SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 2002

AN 2002-360285 JAPIO
AB PROBLEM TO BE SOLVED: To provide a desired vaccine without having an infecting capacity, capable of easily being produced and giving a protection against the infection of **Babesia canis**, preferably against the whole strains of **Babesia canis**.
SOLUTION: This vaccine for protecting the infection of **Babesia canis** is prepared by using nucleic acid sequences encoding new **Babesia canis** associated proteins, a cDNA fragment containing these sequences, a recombinant DNA molecule, a live recombinant carrier, proteins encoded by these nucleotide sequences or a gene material encoding these proteins. Also, these materials can be used as diagnostic tools for detecting a **Babesia canis** associated nucleic acid, a **Babesia canis** associated antigen and an antibody against a **Babesia canis** associated antigenic material.

FILE 'HOME' ENTERED AT 10:18:43 ON 21 NOV 2003

(FILE 'USPATFULL' ENTERED AT 10:49:30 ON 25 NOV 2003)

L1 91 SEA FILE=USPATFULL ABB=ON PLU=ON (BABESIA OR B)(W)CANIS

L2 13 SEA FILE=USPATFULL ABB=ON PLU=ON L1(L)(15KD? OR 15KILOD? OR KILOD? OR KILO(W)(DA OR DALTON) OR KDA? OR 15K)

L2 ANSWER 1 OF 13 USPATFULL on STN

ACCESSION NUMBER: 2003:237715 USPATFULL

TITLE: Babesia canis vaccine

INVENTOR(S): Schetters, Theodorus Petrus Maria, Cuyk, NETHERLANDS
Carcy, Bernard Pierre Dominique, Montpellier, FRANCE
Drakulovski, Pascal Robert, Montpellier, FRANCE

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003165872	A1	20030904	
APPLICATION INFO.:	US 2002-87573	A1	20020228	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-200816	20010603

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: INTERVET INC, 405 STATE STREET, PO BOX 318, MILLSBORO, DE, 19966

NUMBER OF CLAIMS: 22

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Page(s)

LINE COUNT: 1761

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to nucleic acid sequences encoding novel Babesia canis associated proteins and to cDNA fragments, recombinant DNA molecules and live recombinant carriers comprising these sequences. Furthermore, the invention relates to host cells comprising such nucleic acid sequences, cDNA fragments, recombinant DNA molecules and live recombinant carriers. Also, the invention relates to proteins encoded by these nucleotide sequences, to vaccines for combating Babesia canis infections comprising these proteins or genetic material encoding these proteins and methods for the preparation of vaccines. Another embodiment of the invention relates to these Babesia canis associated proteins for use in vaccines and to the use of the Babesia canis associated proteins in the manufacture of vaccines. Finally the invention relates to diagnostic tools for the detection of Babesia canis associated nucleic acid sequences, for the detection of Babesia canis associated antigens and for the detection of antibodies against Babesia canis associated antigenic material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/006.000
INCLS: 435/069.300; 435/183.000; 435/320.100; 435/258.100; 424/191.100; 536/023.700

NCL NCLM: 435/006.000
NCLS: 435/069.300; 435/183.000; 435/320.100; 435/258.100;

424/191.100; 536/023.700

L2 ANSWER 2 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2003:200467 USPATFULL
TITLE: Chimeric gene formed of the DNA sequences that encode the antigenic determinants of four proteins of L. infantum, useful for serologic diagnosis of canine Leishmaniosis and protein obtained
INVENTOR(S): Alonso Bedate, Carlos, Madrid, SPAIN
Requena Rolania, Jose Maria, Madrid, SPAIN
Soto Alvarez, Manuel, Madrid, SPAIN
PATENT ASSIGNEE(S): C.B.F. LETI S.A., MADRID, SPAIN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003138451	A1	20030724
APPLICATION INFO.:	US 2003-337312	A1	20030107 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-788345, filed on 21 Feb 2001, GRANTED, Pat. No. US 6525186
Continuation-in-part of Ser. No. US 1998-219306, filed on 23 Dec 1998, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 957
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Chimeric gene formed by the DNA sequences that encode the antigenic determinants of four proteins of L. infantum, useful for the serological diagnosis of canine Leishmaniosis and protein obtained, that consists of the prior employment of a cloning strategy. The patent describes the intermediate products generated during the process. A clone is achieved expressed in the protein rLiPO-Ct-Q (pPQI). To this initial vector, by means of the use of suitable restriction targets, DNA fragments are sequentially added that are encoded in other proteins and after each cloning step the correct orientation of each one of the inserts reduces the size of the expression products, the complete nucleotide sequence of the final pPQV clone being determined. A polypeptide is obtained with a molecular mass of 38 kD and with an isoelectric point of 7.37.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/191.100
INCLS: 530/350.000
NCL NCLM: 424/191.100
NCLS: 530/350.000

L2 ANSWER 3 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2003:119685 USPATFULL
TITLE: Protein from brucella species
INVENTOR(S): Lindler, Luther E., Wheaton, MD, UNITED STATES
Warren, Richard, Blue Bell, PA, UNITED STATES
VanDeVerg, Lillian, Gaithersburg, MD, UNITED

STATES
Rubin, Fran, Bethesda, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003082170	A1	20030501
APPLICATION INFO.:	US 2001-785689	A1	20010220 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-82535, filed on 21 May 1998, ABANDONED Continuation-in-part of Ser. No. US 1995-446103, filed on 19 May 1995, ABANDONED

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Elizabeth Arwine, Patent Attorney, U.S. Army Medical Research & Materiel Command, 504 Scott Street, Fort Detrick, MD, 21702-5012

NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 339
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A 28 kDa protein which has use as a diagnostic agent for identifying antibodies to Brucella species and as vaccines to raise antibodies against several species of Brucella has been purified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/130.100
INCLS: 530/350.000; 514/002.000; 435/070.210
NCL NCLM: 424/130.100
NCLS: 530/350.000; 514/002.000; 435/070.210

L2 ANSWER 4 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2003:64311 USPATFULL
TITLE: Over-expressing homologous antigen vaccine and a method of making the same
INVENTOR(S): Schurig, Gerhardt, Blacksburg, VA, UNITED STATES
Boyle, Stephen M., Blacksburg, VA, UNITED STATES
Sriranganathan, Nammalwar, Blacksburg, VA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003044431	A1	20030306
APPLICATION INFO.:	US 2002-268673	A1	20021011 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-692621, filed on 20 Oct 2000, PENDING Division of Ser. No. US 1998-91521, filed on 19 Jun 1998, GRANTED, Pat. No. US 6149920 A 371 of International Ser. No. WO 1997-US23032, filed on 5 Dec 1997, PENDING

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Technology Law Offices, P.O. Box 818, Middleburg, VA, 20118

NUMBER OF CLAIMS: 60
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 858
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to an over-expressing homologous antigen vaccine, a method of producing the same, and use of the vaccine for prophylaxis or treatment of vertebrates at risk of or suffering from disease caused by a pathogenic micro-organism. The vaccine is an attenuated or avirulent pathogenic micro-organism that over-expresses at least one homologous antigen encoded by at least one gene derived from the pathogenic micro-organism, and may also express a heterologous antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/252.100
INCLS: 424/200.100
NCL NCLM: 424/252.100
NCLS: 424/200.100

L2 ANSWER 5 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2002:266438 USPATFULL
TITLE: Chimeric gene formed of the DNA sequences that encode the antigenic determinants of four proteins of L. infantum, useful for serologic diagnosis of canine leishmaniosis and protein obtained
INVENTOR(S): Bedate, Carlos Alonso, Madrid, SPAIN
Requena Rolania, Jose Maria, Madrid, SPAIN
Soto Alvarez, Manuel, Madrid, SPAIN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002147321	A1	20021010
	US 6525186	B2	20030225
APPLICATION INFO.:	US 2001-788345	A1	20010221 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-219306, filed on 23 Dec 1998, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Chimeric gene formed by the DNA sequences that encode the antigenic determinants of four proteins of L. infantum, useful for the serological diagnosis of canine Leishmaniosis and protein obtained, that consists of the prior employment of a cloning strategy. The patent describes the intermediate products generated during the process. A clone is achieved expressed in the protein rLiPO-Ct-Q (pPQI). To this initial vector, by means of the use of suitable restriction targets, DNA fragments are sequentially added that are encoded in other proteins and after each cloning step the correct orientation of each one of the inserts reduces the size of the expression products, the complete nucleotide sequence of the final pPQV clone being determined. A polypeptide is obtained with a molecular mass of 38 kD and with an isoelectric point of 7.37.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 536/023.200

INCLS: 435/006.000; 435/007.220; 435/189.000; 435/320.100; 435/258.300
NCL NCLM: 536/023.400
NCLS: 424/184.100; 424/191.100; 424/192.100; 424/265.100; 424/269.100; 435/006.000; 435/007.100; 435/069.700; 435/350.000; 530/300.000; 530/350.000; 536/023.100

L2 ANSWER 6 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2002:254050 USPATFULL
TITLE: CHIMERIC GENE FORMED BY THE DNA SEQUENCES THAT ENCODE THE ANTIGENIC DETERMINANTS OF FOUR PROTEINS OF L. INFANTUM AND PROTEIN ENCODED BY SAID GENE, AND PHARMACUETICAL COMPOSITION USEFUL FOR PREVENTING AND/OR TREATING LEISHMANIOSIS IN ANIMALS OR HUMANS
INVENTOR(S): Bedate, Carlos Alonso, Madrid, SPAIN
Requena Rolania, Jose Maria, Madrid, SPAIN
Soto Alvarez, Manuel, Madrid, SPAIN
PATENT ASSIGNEE(S): C.B.F. Leti S.A., Madrid, SPAIN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6458359	B1	20021001	
APPLICATION INFO.:	US 1999-471396		19991223	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-113825P	19981223 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Smith, Lynette R. F.
ASSISTANT EXAMINER: Baskar, Padmavathi
LEGAL REPRESENTATIVE: Browdy and Neimark, P.L.L.C.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 1852
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A chimeric polypeptide encoded by the chimeric gene formed by the DNA sequences that encode the antigenic determinants of four proteins of L. infantum is disclosed. The protein obtained, rLiPO-Ct-Q (pPQI) has a molecular mass of 38 kD with an isoelectric point of 7.37. This chimeric polypeptide is useful for preventing and/or treating leishmaniosis in animals or humans.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/192.100
INCLS: 424/185.100; 424/192.100; 424/193.100; 424/200.100; 424/269.100; 424/191.100; 530/300.000; 530/350.000; 530/324.000; 530/333.000; 530/334.000; 530/344.000; 530/403.000; 530/412.000; 435/007.100; 435/007.220; 435/007.400; 435/007.920; 435/069.100; 435/069.300; 435/069.700; 435/071.100
NCL NCLM: 424/192.100
NCLS: 424/185.100; 424/191.100; 424/193.100; 424/200.100; 424/269.100; 435/007.100; 435/007.220; 435/007.400; 435/007.920; 435/069.100; 435/069.300; 435/069.700;

435/071.100; 530/300.000; 530/324.000; 530/333.000;
530/334.000; 530/344.000; 530/350.000; 530/403.000;
530/412.000

L2 ANSWER 7 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2002:148266 USPATFULL
TITLE: RECOMBINANT PROTEIN CONTAINING A C-TERMINAL FRAGMENT OF PLASMODIUM MSP-1
INVENTOR(S): LONGACRE-ANDRE, SHIRLEY, PARIS, FRANCE
ROTH, CHARLES, RUEIL MALMAISON, FRANCE
NATO, FARIDABANO, ANTONY, FRANCE
BARNWELL, JOHN W., STONE MOUNTAIN, GA, UNITED STATES
MENDIS, KAMINI, COLUMBO, SRI LANKA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002076403	A1	20020620
APPLICATION INFO.:	US 1998-134333	A1	19980814 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1997-FR290, filed on 14 Feb 1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1996-1822	19960214

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
NUMBER OF CLAIMS: 67
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 59 Drawing Page(s)
LINE COUNT: 2266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a recombinant protein fabricated in a baculovirus system, of which the essential constitutive polypeptide sequence is that of a C-terminal fragment of 19 kilodalton (p19) of the surface protein 1 (protein MSP-1) of the merozoite parasite of the Plasmodium type, particularly Plasmodium falciparum, which is infectious for humans, said C-terminal fragment remaining normally anchored at the surface of the parasite at the end of its penetration phase into human erythrocytes in the occurrence of an infectious cycle. Said recombinant protein is applicable to the production of vaccines against malaria.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/130.100
INCLS: 435/069.100; 530/350.000; 435/325.000; 435/326.000; 536/023.500; 424/093.100; 424/204.100
NCL NCLM: 424/130.100
NCLS: 435/069.100; 530/350.000; 435/325.000; 435/326.000; 536/023.500; 424/093.100; 424/204.100

L2 ANSWER 8 OF 13 USPATFULL on STN
ACCESSION NUMBER: 2002:48024 USPATFULL
TITLE: NOVEL VACCINES AND PHARMACEUTICAL COMPOSITIONS

	USING MEMBRANE VESICLES OF MICROORGANISMS, AND METHODS FOR PREPARING SAME
INVENTOR(S):	KADURUGAMUWA, JAGATH L., GUELPH, CANADA BEVERIDGE, TERRY J., ELORA, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002028215	A1	20020307	
APPLICATION INFO.:	US 1999-370860	A1	19990809	(9)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	DOUGLAS P MUELLER, MERCHANT & GOULD PC, 3100 NORWEST CENTER, 90 SOUTH SEVENTH STREET, MINNEAPOLIS, MN, 55402
NUMBER OF CLAIMS:	17
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	35 Drawing Page(s)
LINE COUNT:	2647

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel vaccines and pharmaceutical compositions using membrane vesicles of microorganisms, methods for preparing same, and their use in the prevention and treatment of infectious diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL	INCLM:	424/234.100
NCL	NCLM:	424/234.100

L2 ANSWER 9 OF 13 USPATFULL on STN

ACCESSION NUMBER:	2001:147456 USPATFULL
TITLE:	Cell lines infected with granulocytic ehrlichia, vaccines, diagnostics and methods
INVENTOR(S):	Coughlin, Richard T., Leicester, MA, United States Gingrich-Baker, Cindy, Boylston, MA, United States
PATENT ASSIGNEE(S):	Aquila Biopharmaceuticals, Inc., Framingham, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6284238	B1	20010904	
APPLICATION INFO.:	US 1995-470358		19950606	(8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Swartz, Rodney P.
LEGAL REPRESENTATIVE:	Pennie & Edmonds LLP
NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	902

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates, in general, to granulocytic Ehrlichia. In particular, the present invention relates to a human promyelocytic leukemia cell line infected with granulocytic Ehrlichia, a method of continually growing granulocytic Ehrlichia, vaccines comprising granulocytic Ehrlichia or granulocytic Ehrlichia antigens, methods of preventing ehrlichiosis in an

animal, antibodies to granulocytic Ehrlichia, and methods for identifying granulocytic Ehrlichia in an animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/088.000
INCLS: 424/088.000; 424/092.000; 435/243.100
NCL NCLM: 424/234.100

L2 ANSWER 10 OF 13 USPATFULL on STN
ACCESSION NUMBER: 1999:137009 USPATFULL
TITLE: Cell lines infected with granulocytic ehrlichia, vaccines, diagnostics and methods
INVENTOR(S): Coughlin, Richard T., Leicester, MA, United States
Gingrich-Baker, Cindy, Boylston, MA, United States
PATENT ASSIGNEE(S): Aquila Biopharmaceuticals, Inc., Framingham, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5976860		19991102
APPLICATION INFO.:	US 1996-613415		19960311 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-470358, filed on 6 Jun 1995		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Housel, James C.
ASSISTANT EXAMINER: Swartz, Rodney P.
LEGAL REPRESENTATIVE: Hale and Dorr LLP
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1235
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates, in general, to granulocytic Ehrlichia. In particular, the present invention relates to a cell line selected from the group consisting of a promyelocytic leukemia cell line, an acute myelogenous leukemia cell line, a histiocytic lymphoma cell line, a monocyte macrophage-like cell line, an acute monocytic leukemia cell line, and an embryonic lung cell line wherein the cell line is infected with granulocytic Ehrlichia, a method of continually growing granulocytic Ehrlichia, vaccines comprising granulocytic Ehrlichia or granulocytic Ehrlichia antigens, methods of preventing ehrlichiosis in an animal, antibodies to granulocytic Ehrlichia, and methods for identifying granulocytic Ehrlichia in an animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/240.200
INCLS: 435/240.100; 435/243.000; 435/252.100; 435/260.000
NCL NCLM: 435/366.000
NCLS: 435/243.000; 435/252.100; 435/260.000; 435/372.000; 435/372.100

L2 ANSWER 11 OF 13 USPATFULL on STN
ACCESSION NUMBER: 1999:12787 USPATFULL
TITLE: Control of parasites

INVENTOR(S): Atkinson, Howard John, Leeds, Great Britain
Koritsas, Vas Michael, Leeds, Great Britain
Lee, Donald Lewis, Leeds, Great Britain
MacGregor, Andrew Neilson, Canterbury, Great Britain
Smith, Judith Elizabeth, Leeds, Great Britain

PATENT ASSIGNEE(S): The University of Leeds, Leeds, England (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5863775		19990126	
	WO 9523229		19950831	
APPLICATION INFO.:	US 1996-702682		19961220	(8)
	WO 1995-GB419		19950228	
			19961220	PCT 371 date
			19961220	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1994-3819	19940228

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy
LEGAL REPRESENTATIVE: Barrett, William A., Hultquist, Steven J.
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1906
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of combating an animal parasite in a host which comprises delivering an anti-parasitic protein to the parasite or to a locus thereof by administering the protein to the host animal as a medicament or as a food. The anti-parasitic protein may be an inhibitor of an enzyme of the parasite, for example an inhibitor of a digestive enzyme such as a cysteine protease inhibitor. The parasite may be a helminth or a protozoan, for example, a nematode. According to one embodiment the anti-parasitic protein is expressed in a transgenic plant which may be a dietary crop for the host animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/172.300
INCLS: 435/069.100; 435/069.200; 435/410.000; 435/412.000; 514/002.000; 800/205.000
NCL NCLM: 424/094.100
NCLS: 435/069.100; 435/069.200; 435/410.000; 435/412.000; 435/468.000; 514/002.000

L2 ANSWER 12 OF 13 USPATFULL on STN
ACCESSION NUMBER: 94:17929 USPATFULL
TITLE: Method for intensive, in vitro culture of Babesia divergens strains

INVENTOR(S): Schrevel, Joseph, Lussac-les-Chateaux, France
Gorenflot, Andre, Gif-sur-Yvette, France
Precigout, Eric, Poitiers, France
Marchand, Alain, Carquefou, France
Brasseur, Philippe, Rouen, France

PATENT ASSIGNEE(S):	L'Hostis, Monique, Nantes, France Rigomier, Daniel, Poitiers, France Valentin, Alexis, Poitiers, France Vidor, Emmanuel, Lyons, France Bissuel, Guy, Le Bois-d'Oingt Chanrion, France Rhone Merieux, Lyons, France (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5290688		19940301	
	WO 9108771		19910627	
APPLICATION INFO.:	US 1991-752625		19911017	(7)
	WO 1990-FR934		19901220	
			19911017	PCT 371 date
			19911017	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1989-16890	19891220

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Nucker, Christine M.
ASSISTANT EXAMINER:	Dubrule, Chris
LEGAL REPRESENTATIVE:	Wegner, Cantor, Mueller & Player
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	829

AB Method for the culture of Babesia divergens, characterized in that the Babesia strain is maintained under culture in a culture medium free from serous protein but containing lipoproteins and red blood corpuscles, and a method for preparing exoantigens and a vaccine containing these antigens.

INCL INCLM: 435/007.100
INCLS: 435/070.400; 435/947.000; 435/249.000; 435/258.100; 424/088.000
NCL NCLM: 435/071.100
NCLS: 424/266.100; 424/270.100; 435/070.400; 435/249.000; 435/258.100; 435/947.000

L2 ANSWER 13 OF 13 USPATFULL on STN

ACCESSION NUMBER:	93:108986 USPATFULL
TITLE:	Polypetides, antigens or vaccines protective against babesiosis
INVENTOR(S):	Gale, Kevin G., Brisbane, Australia Waltisbuhl, David J., Queensland, Australia Wright, Ian G., Brisbane, Australia Goodger, Brian V., New South Wales, Australia
PATENT ASSIGNEE(S):	Commonwealth Scientific & Industrial, United States (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5273884		19931228	
APPLICATION INFO.:	US 1990-470284		19900125	(7)

Searcher : Shears 308-4994

	NUMBER	DATE
PRIORITY INFORMATION:	AU 1989-2427	19890125
	AU 1989-7722	19891116
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Zitomer, Stephanie W.	
LEGAL REPRESENTATIVE:	Sughrue, Mion Zinn Macpeak & Seas	
NUMBER OF CLAIMS:	43	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	20 Drawing Figure(s); 21 Drawing Page(s)	
LINE COUNT:	1771	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An antigen which produces immunity against homologous or heterologous challenge with babesia of cattle. The antigen is immunoreactive with a monoclonal antibody or polyclonal antisera recognising a protein located on the surface of babesia-infected erythrocytes and within a spherical or mitochondrion like organelle. The antigen can be prepared by (i) preparing nucleic acids from babesia infected erythrocytes depleted of leucocytes; (ii) forming a cDNA or genomic library from nucleic acids obtained in step (i); (iii) screening said library formed in step (ii) with a suitable probe to identify clones of interest; and thus providing DNA inserts for an expression vector which may be used to transform an appropriate host; (iv) obtaining a recombinant polypeptide from said transformed hosts which is protective against babesiosis. A monoclonal antibody reactive with the antigen, a DNA sequence which produces a protein protective against babesiosis when administered as a vaccine, and a vaccine including the antigen in combination with an adjuvant is also included in the inventive concept.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/007.100
INCLS: 424/088.000; 435/007.220; 435/069.100; 530/388.100; 530/388.600; 530/350.000; 536/023.100

NCL NCLM: 424/191.100
NCLS: 424/266.100; 424/270.100; 435/007.220; 435/069.100; 530/350.000; 530/388.100; 530/388.600; 536/023.100

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